

10/513699

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEAL1624

PASSWORD:

\*\*\*\*\* RECONNECTED TO STN INTERNATIONAL \*\*\*\*\*  
SESSION RESUMED IN FILE 'CAPLUS' AT 11:28:57 ON 01 FEB 2008  
FILE 'CAPLUS' ENTERED AT 11:28:57 ON 01 FEB 2008  
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)  
COST IN U.S. DOLLARS

	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	103.89	282.46

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-13.60	-13.60

=> file casreact  
COST IN U.S. DOLLARS

	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	104.85	283.42

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-13.60	-13.60

FILE 'CASREACT' ENTERED AT 11:30:01 ON 01 FEB 2008  
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FILE CONTENT:1840 - 26 Jan 2008 VOL 148 ISS 5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

\*\*\*\*\*  
\* CASREACT now has more than 13.8 million reactions \*  
\*  
\*\*\*\*\*

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

<12/04/2007>

Erich Leese

10/513699

=>

Uploading C:\Program Files\Stnexp\Queries\10524517\last.str



```
chain nodes :
7 8 9 11 12 14 15 18 19 20 21
ring nodes :
1 2 3 4 5 6
ring/chain nodes :
16 22
chain bonds :
1-7 2-15 3-14 5-11 6-12 7-8 7-9 9-16 18-19 18-22 19-20 19-21
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-2 1-6 1-7 2-3 2-15 3-4 3-14 4-5 5-6 5-11 6-12 7-8 7-9 9-16 18-19
18-22 19-21
exact bonds :
19-20
isolated ring systems :
containing 1 :
```

G1:C,H,O,X

```
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 11:CLASS
12:CLASS 14:CLASS 15:CLASS 16:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS
22:CLASS
fragments assigned product role:
containing 1
fragments assigned reactant/reagent role:
containing 18
```

L5 STRUCTURE UNLOADED

<12/04/2007>

Erich Leese

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=> s 15

SAMPLE SEARCH INITIATED 11:30:31 FILE 'CASREACT'  
SCREENING COMPLETE - 502 REACTIONS TO VERIFY FROM 24 DOCUMENTS  
100.0% DONE 502 VERIFIED 101 HIT RXNS 10 DOCS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED VERIFICATIONS: 8697 TO 11383  
PROJECTED ANSWERS: 11 TO 389

L6 10 SEA SSS SAM L5 ( 101 REACTIONS)

=> s 15 full

FULL SEARCH INITIATED 11:30:50 FILE 'CASREACT'  
SCREENING COMPLETE - 8697 REACTIONS TO VERIFY FROM 561 DOCUMENTS  
100.0% DONE 8697 VERIFIED 1974 HIT RXNS 197 DOCS  
SEARCH TIME: 00.00.02

L7 197 SEA SSS FUL L5 ( 1974 REACTIONS)

=> s 17 and py<2003

486994 PY<2003

L8 93 L7 AND PY<2003

=> s 18 and organic solvent

12293 ORGANIC

21 ORGANICS

12313 ORGANIC  
(ORGANIC OR ORGANICS)

62178 SOLVENT

18894 SOLVENTS

71620 SOLVENT  
(SOLVENT OR SOLVENTS)

743 ORGANIC SOLVENT  
(ORGANIC(W) SOLVENT)

L9 0 L8 AND ORGANIC SOLVENT

=> s 18 and solvent

62178 SOLVENT

18894 SOLVENTS

71620 SOLVENT  
(SOLVENT OR SOLVENTS)

L10 1 L8 AND SOLVENT

=> d ibib abs hit

10/513699

L10 ANSWER 1 OF 1 CASREACT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 138:55769 CASREACT

TITLE: Synthesis of potent and highly selective inhibitors of human trypsin

AUTHOR(S): Slusarchyk, William A.; Bolton, Scott A.; Hartl, Karen S.; Huang, Ming-Hsing; Jacobs, Glenn; Meng, Wei; Ogletree, Martin L.; Pi, Zulan; Schumacher, William A.; Seiler, Steven M.; Sutton, James C.; Treuner, Uwe; Zahler, Robert; Zhao, Guohua; Bisacchi, Gregory S.

CORPORATE SOURCE: The Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08543-4000, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(21), 3235-3238

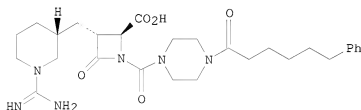
CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

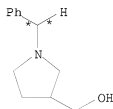
GI



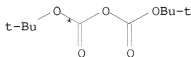
I

AB The serine protease trypsin is implicated in allergic and inflammatory diseases and associated with asthma. The synthesis and SAR of a series of N1-activated-4-carboxy azetidinones are described, resulting in identification of BMS-363131 (I) as a potent inhibitor of human trypsin ( $IC_{50} < 1.7$  nM) with high selectivity (>3000-fold) for trypsin vs. related serine proteases including trypsin.

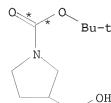
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

$$\text{RX(7) OF 275} \quad \text{AD} + \text{AE} \implies \text{AF} \dots$$


AD



AE



AF

(7)  $\rightarrow$

RX(7) RCT AD 5731-17-9

<12/04/2007>

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STAGE(1)

RGT S 1333-74-0 H2  
CAT 7440-05-3 Pd  
SOL 67-56-1 MeOH

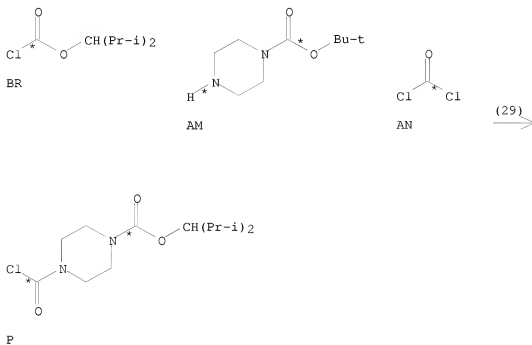
STAGE(2)

RCT AE 24424-99-5  
SOL 109-99-9 THF

PRO AF 114214-69-6

NTE isopropanol may also be used as a solvent in the first stage

RX(29) OF 275 BR + AM + AN ==> P...



RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et3N

<12/04/2007>

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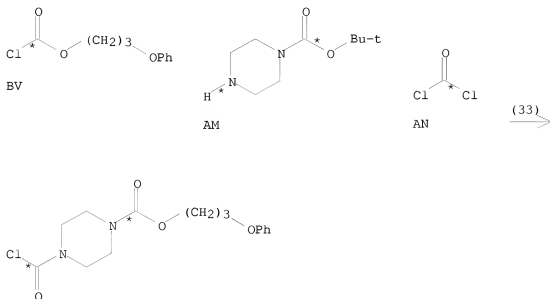
10/513699

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(33) OF 275 BV + AM + AN ==> BK...



BK

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

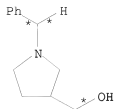
RX(50) OF 275 COMPOSED OF RX(7), RX(8)

RX(50) AD + AE ==> AH

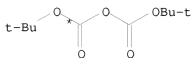
<12/04/2007>

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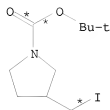


AD



AE

2  
STEPS  
→



AH

RX(7) RCT AD 5731-17-9

STAGE(1)

RGT S 1333-74-0 H2

CAT 7440-05-3 Pd

SOL 67-56-1 MeOH

STAGE(2)

RCT AE 24424-99-5

SOL 109-99-9 THF

PRO AF 114214-69-6

NTE isopropanol may also be used as a solvent in the first stage

RX(8) RCT AF 114214-69-6

RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole

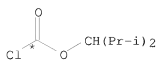
PRO AH 479622-36-1

SOL 75-09-2 CH2Cl2

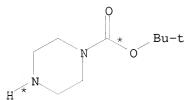
RX(75) OF 275 COMPOSED OF RX(29), RX(4)

RX(75) BR + AM + AN + L ==> Q

10/513699



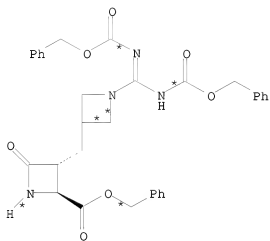
BR



AM



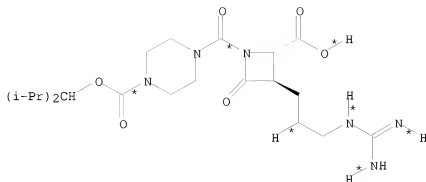
AN



L

2  
STEPS  
→





Q

RX(29) RCT BR 30250-57-8, AM 57260-71-6

## STAGE(1)

RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

## STAGE(2)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

## STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(4) RCT L 253177-00-3, P 253177-45-6

## STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

## STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO Q 253173-70-5

RX(76) OF 275 COMPOSED OF RX(29), RX(5)

RX(76) BR + AM + AN + X ==&gt; Y



$\text{---CH(Pr-i)}_2$ 

Y

YIELD 82%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(5) RCT P 253177-45-6, X 384830-18-6

RGT N 121-44-8 Et3N

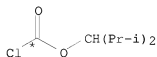
PRO Y 253177-10-5

CAT 1122-58-3 4-DMAP

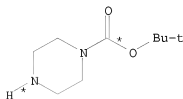
SOL 68-12-2 DMF

RX(77) OF 275 COMPOSED OF RX(29), RX(20)

RX(77) BR + AM + AN + BA ==&gt; BB



BR

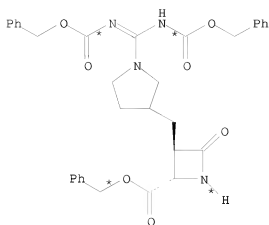


AM



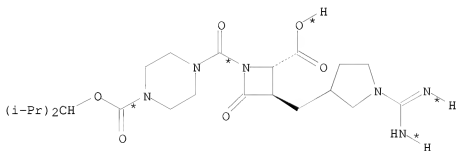
AN

10/513699



BA

2  
STEPS  
→



BB

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

<12/04/2007>

Erich Leese

10/513699

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(20) RCT BA 479622-23-6, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP

SOL 68-12-2 DMF

STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl

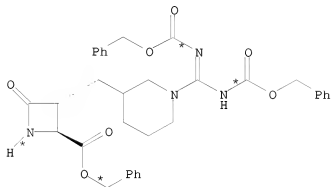
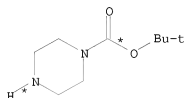
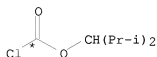
CAT 7440-05-3 Pd

SOL 123-91-1 Dioxane, 7732-18-5 Water

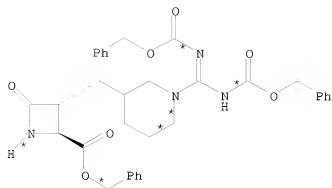
PRO BB 479622-24-7

RX(78) OF 275 COMPOSED OF RX(29), RX(21)

RX(78) 4 BR + 4 AM + 4 AN + 4 X ==> BB + BC  
+ BD + BE

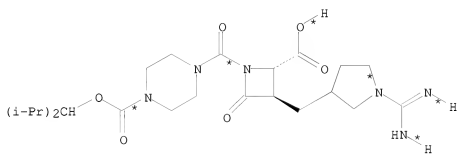


10/513699

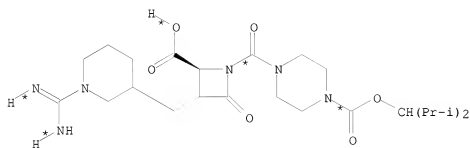


X

2  
STEPS  
→



BB

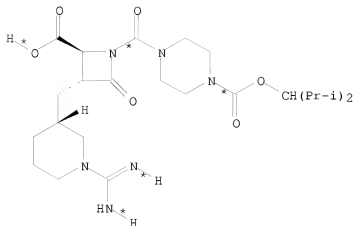


BC

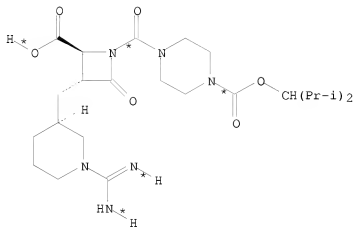
<12/04/2007>

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BD



BE

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

<12/04/2007>

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10/513699

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(21) RCT X 384830-18-6, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP

SOL 68-12-2 DMF

STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl

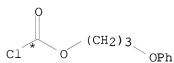
CAT 7440-05-3 Pd

SOL 123-91-1 Dioxane, 7732-18-5 Water

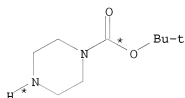
PRO BB 479622-24-7, BC 253177-54-7, BD 479622-25-8, BE  
479622-26-9

RX(84) OF 275 COMPOSED OF RX(33), RX(25)

RX(84) BV + AM + AN + X ==> BL



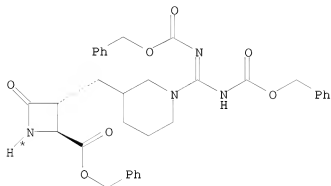
BV



AM



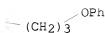
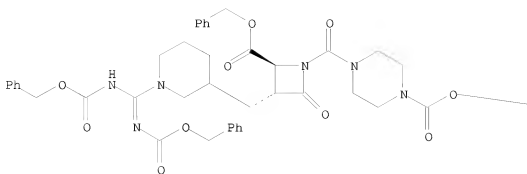
AN



X

2  
STEPS  
=>





BL  
YIELD 82%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6

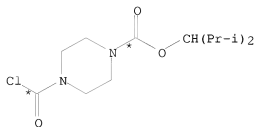
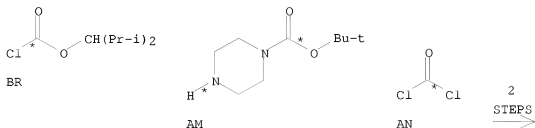
RGT N 121-44-8 Et3N  
PRO BL 384830-26-6  
CAT 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

10/513699

RX(93) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(4)  
AND REACTION SEQUENCE RX(3), RX(4)

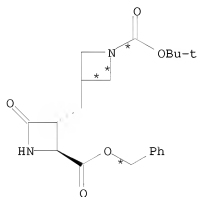
... BR + AM + AN ==> P...

...G + K + P ==> Q

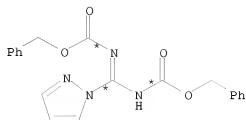


P

START NEXT REACTION SEQUENCE



G

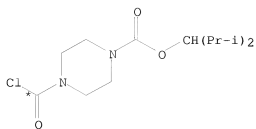


K

<12/04/2007>

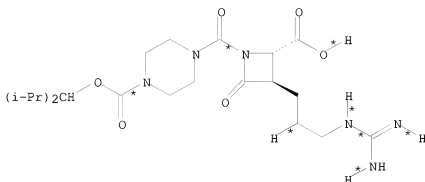
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10/513699



P

2  
STEPS  
→



Q

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(3) RCT G 253176-97-5

STAGE(1)

RGT M 76-05-1 F3CCO2H

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SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

PRO L 253177-00-3

NTE alternative prepn. shown

RX(4) RCT L 253177-00-3, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP

SOL 68-12-2 DMF

STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl

CAT 7440-05-3 Pd

SOL 123-91-1 Dioxane, 7732-18-5 Water

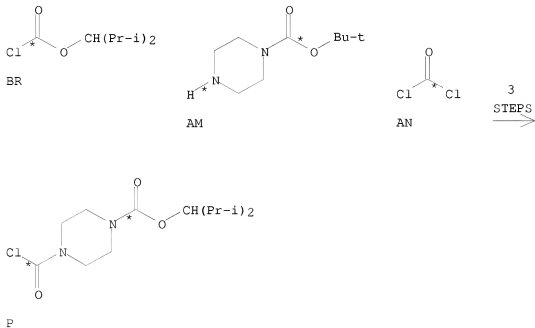
PRO Q 253173-70-5

RX(94) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(4)

AND REACTION SEQUENCE RX(2), RX(3), RX(4)

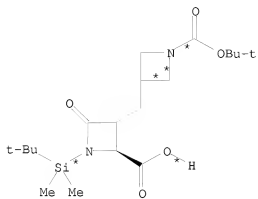
... BR + AM + AN ==> P...

...C + F + K + P ==> Q



START NEXT REACTION SEQUENCE

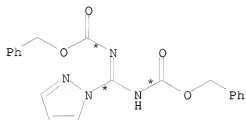
10/513699



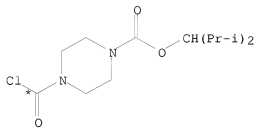
C



F



K

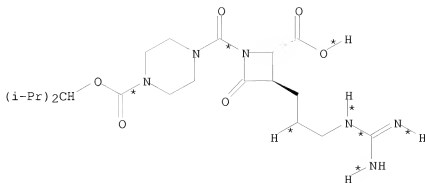


P

3  
STEPS  
→

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Q

RX(29) RCT BR 30250-57-8, AM 57260-71-6

## STAGE(1)

RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

## STAGE(2)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

## STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(2) RCT C 253176-95-3

## STAGE(1)

RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

## STAGE(2)

RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO G 253176-97-5

RX(3) RCT G 253176-97-5

## STAGE(1)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

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STAGE(2)

RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO L 253177-00-3  
NTE alternative prepn. shown

RX(4) RCT L 253177-00-3, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

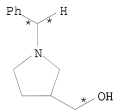
STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

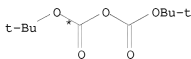
PRO Q 253173-70-5

RX(96) OF 275 COMPOSED OF RX(7), RX(8), RX(43)

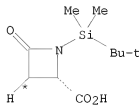
RX(96) AD + AE + B ==> AX



AD

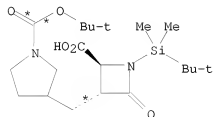


AE



B

3  
STEPS  
=>



AX

RX(7) RCT AD 5731-17-9

STAGE(1)

RGT S 1333-74-0 H2  
CAT 7440-05-3 Pd

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SOL 67-56-1 MeOH

STAGE(2)

RCT AE 24424-99-5

SOL 109-99-9 THF

PRO AF 114214-69-6

NTE isopropanol may also be used as a solvent in the first stage

RX(8)

RCT AF 114214-69-6

RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole

PRO AH 479622-36-1

SOL 75-09-2 CH2Cl2

RX(43)

RCT AH 479622-36-1, B 82938-50-9

RGT D 4111-54-0 LiN(Pr-i)2

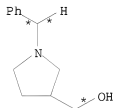
PRO AX 479622-21-4

SOL 109-99-9 THF

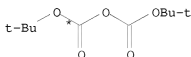
NTE stereoselective

RX(98) OF 275 COMPOSED OF RX(7), RX(8), RX(43), RX(16)

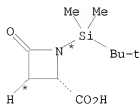
RX(98) AD + AE + B + F ==> AY



AD



AE

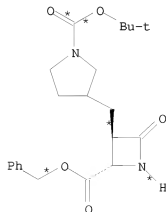


B



F

4  
STEPS  
=>



AY



RX(7) RCT AD 5731-17-9

## STAGE(1)

RGT S 1333-74-0 H2  
 CAT 7440-05-3 Pd  
 SOL 67-56-1 MeOH

## STAGE(2)

RCT AE 24424-99-5  
 SOL 109-99-9 THF

PRO AF 114214-69-6

NTE isopropanol may also be used as a solvent in the first stage

RX(8) RCT AF 114214-69-6  
 RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole  
 PRO AH 479622-36-1  
 SOL 75-09-2 CH2Cl2

RX(43) RCT AH 479622-36-1, B 82938-50-9  
 RGT D 4111-54-0 LiN(Pr-i)2  
 PRO AX 479622-21-4  
 SOL 109-99-9 THF  
 NTE stereoselective

RX(16) RCT AX 479622-21-4

## STAGE(1)

RGT H 429-41-4 Bu4N.F  
 SOL 109-99-9 THF

## STAGE(2)

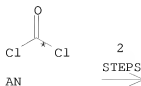
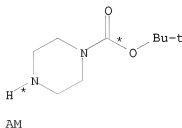
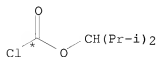
RCT F 100-39-0  
 RGT I 144-55-8 NaHCO3  
 SOL 68-12-2 DMF

PRO AY 479622-22-5

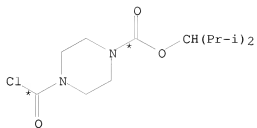
RX(124) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(20)  
 AND REACTION SEQUENCE RX(18), RX(20)

... BR + AM + AN ==&gt; P...

...AY + K + P ==&gt; BB

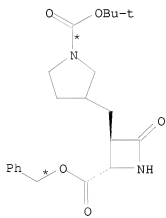


10/513699

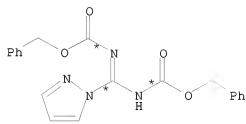


P

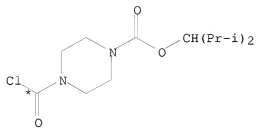
START NEXT REACTION SEQUENCE



AY



K

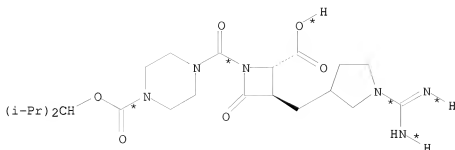


P

2  
STEPS  
→

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BB

RX(29) RCT BR 30250-57-8, AM 57260-71-6

## STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

## STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

## STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(18) RCT AY 479622-22-5

## STAGE(1)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

## STAGE(2)

RCT K 152120-55-3

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

PRO BA 479622-23-6

NTE alternative prepn. shown

RX(20) RCT BA 479622-23-6, P 253177-45-6

## STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP

SOL 68-12-2 DMF

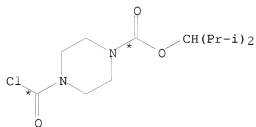
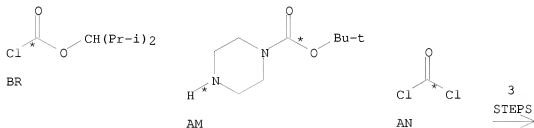
## STAGE(2)

10/513699

RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

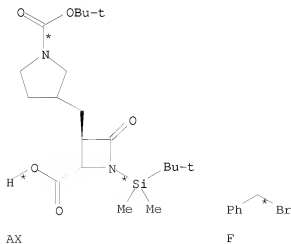
PRO BB 479622-24-7

RX(125) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(20)  
AND REACTION SEQUENCE RX(16), RX(18), RX(20)  
... BR + AM + AN ==> P...  
...AX + F + K + P ==> BB



P

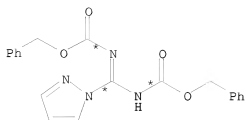
START NEXT REACTION SEQUENCE



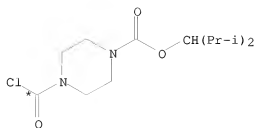
<12/04/2007>

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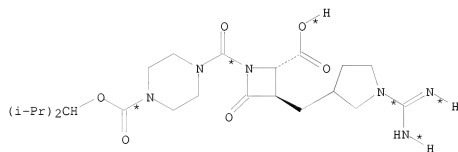


K



P

3  
STEPS  
→



BB

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

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RX(16) RCT AX 479622-21-4

STAGE(1)

RGT H 429-41-4 Bu4N.F

SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0

RGT I 144-55-8 NaHCO3

SOL 68-12-2 DMF

PRO AY 479622-22-5

RX(18) RCT AY 479622-22-5

STAGE(1)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

PRO BA 479622-23-6

NTE alternative prepn. shown

RX(20) RCT BA 479622-23-6, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP

SOL 68-12-2 DMF

STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl

CAT 7440-05-3 Pd

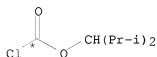
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO BB 479622-24-7

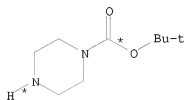
RX(133) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5)  
AND REACTION SEQUENCE RX(19), RX(5)

... BR + AM + AN ==> P...

...AZ + K + P ==> Y



BR



AM



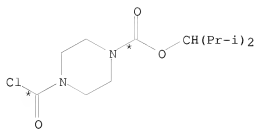
AN

2  
STEPS  
→

<12/04/2007>

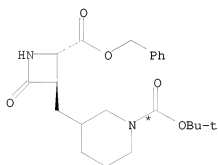
Erich Leese

10/513699

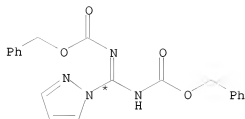


P

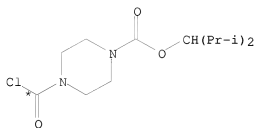
START NEXT REACTION SEQUENCE



AZ

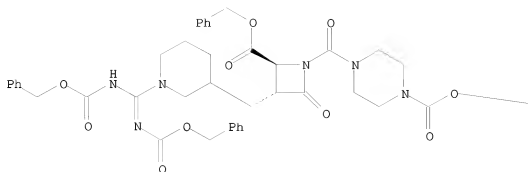


K



P

2  
STEPS  
→



CH(Pr-i)<sub>2</sub>

Y  
YIELD 82%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H



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SOL 75-09-2 CH2C12

STAGE(2)

RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

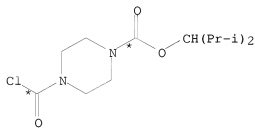
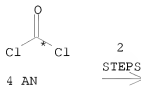
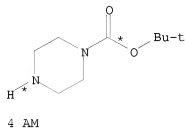
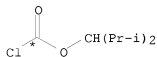
PRO X 384830-18-6  
NTE alternative prepn. shown

RX(5) RCT P 253177-45-6, X 384830-18-6  
RGT N 121-44-8 Et3N  
PRO Y 253177-10-5  
CAT 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

RX(134) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(21)  
AND REACTION SEQUENCE RX(19), RX(21)

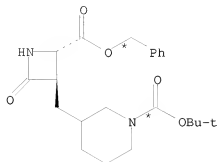
...4 BR + 4 AM + 4 AN ==> P...

...4 AZ + 4 K + 4 P ==> BB + BC + BD + BE

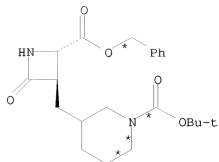


START NEXT REACTION SEQUENCE

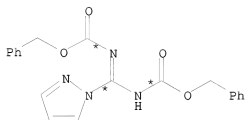
10/513699



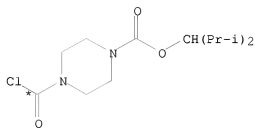
3 AZ



AZ

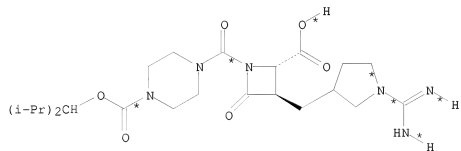


4 K



4 P

2  
STEPS  
→

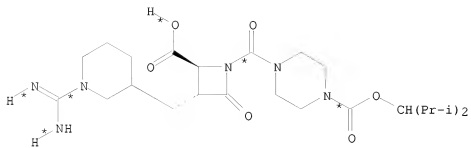


BB

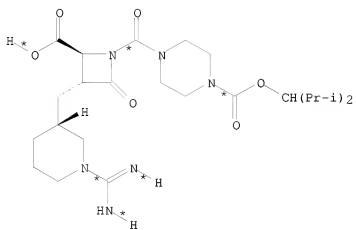
<12/04/2007>

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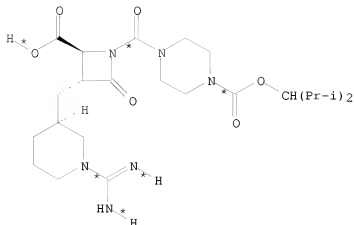


BC



BD

10/513699



BE

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prepn. shown

RX(21) RCT X 384830-18-6, P 253177-45-6

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STAGE(1)

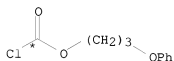
RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

STAGE(2)

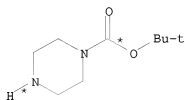
RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO BB 479622-24-7, BC 253177-54-7, BD 479622-25-8, BE  
479622-26-9

RX(138) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25)  
AND REACTION SEQUENCE RX(19), RX(25)  
... BV + AM + AN ==> BK...  
...AZ + K + BK ==> BL



BV

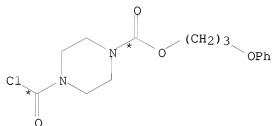


AM



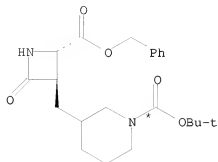
AN

2  
STEPS  
➡

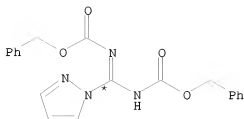


BK

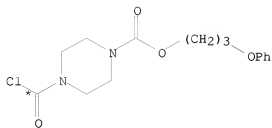
START NEXT REACTION SEQUENCE



AZ



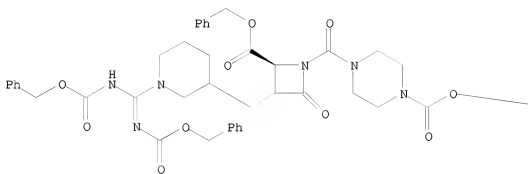
K

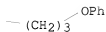


BK

2  
STEPS  
→

PAGE 1-A





BL  
YIELD 82%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6

RGT N 121-44-8 Et3N  
PRO BL 384830-26-6  
CAT 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

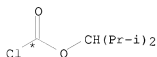
RX(146) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5)

10/513699

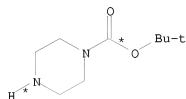
AND REACTION SEQUENCE RX(17), RX(19), RX(5)

... BR + AM + AN ==> P...

...AW + F + K + P ==> Y



BR

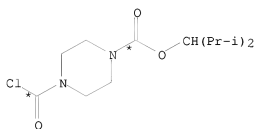


AM



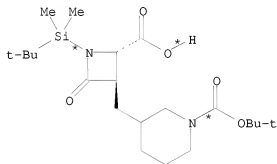
AN

3  
STEPS  
→



P

START NEXT REACTION SEQUENCE



AW



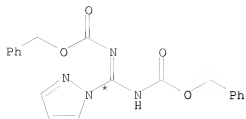
F

<12/04/2007>

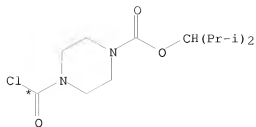
Erich Leese



10/513699



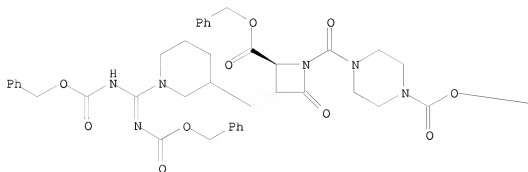
K



P

3  
STEPS  
→

PAGE 1-A



PAGE 1-B

CH(Pr-i)<sub>2</sub>

Y  
YIELD 82%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

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STAGE(1)  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

STAGE(2)  
RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(3)  
RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO P 253177-45-6  
NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(17) RCT AW 253177-04-7

STAGE(1)  
RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

STAGE(2)  
RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)  
RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)  
RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6  
NTE alternative prep. shown

RX(5) RCT P 253177-45-6, X 384830-18-6  
RGT N 121-44-8 Et3N  
PRO Y 253177-10-5  
CAT 1122-58-3 4-DMAF  
SOL 68-12-2 DMF

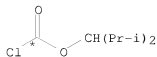
RX(147) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(21)  
AND REACTION SEQUENCE RX(17), RX(19), RX(21)

...4 BR + 4 AM + 4 AN ==> P...  
...4 AW + 4 F + 4 K + 4 P ==> BB + BC + BD + BE

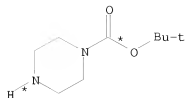
<12/04/2007>

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4 BR

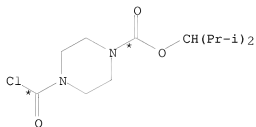


4 AM



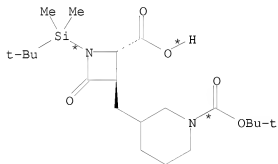
4 AN

3  
STEPS  
➔



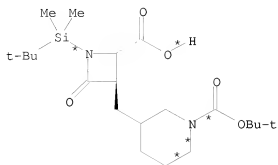
P

START NEXT REACTION SEQUENCE



3 AW

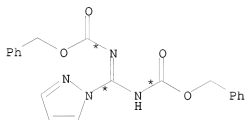
10/513699



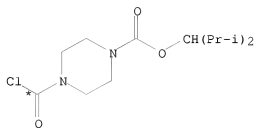
AW



4 F

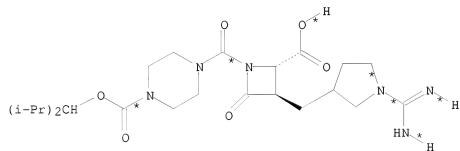


4 K



4 P

3  
STEPS  
→

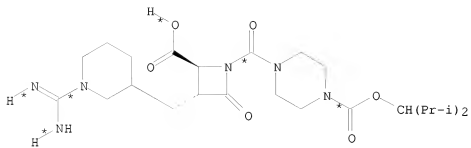


BB

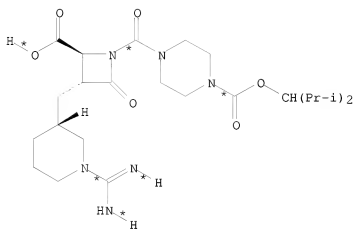
<12/04/2007>

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10/513699

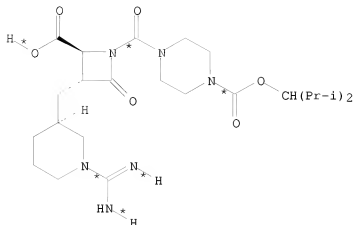


BC



BD

10/513699



BE

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F

SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0

RGT I 144-55-8 NaHCO3

SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

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RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6  
NTE alternative prepn. shown

RX(21) RCT X 384830-18-6, P 253177-45-6

STAGE(1)

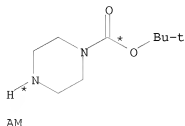
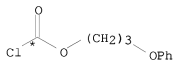
RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

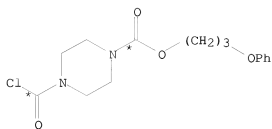
PRO BB 479622-24-7, BC 253177-54-7, BD 479622-25-8, BE  
479622-26-9

RX(151) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25)  
AND REACTION SEQUENCE RX(17), RX(19), RX(25)  
... BV + AM + AN ==> BK...  
...AM + F + K + BK ==> BL



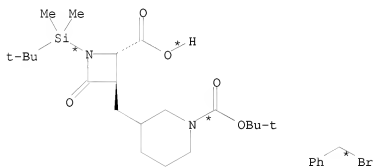
3  
STEPS  
→

10/513699



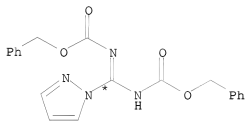
BK

START NEXT REACTION SEQUENCE

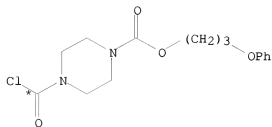


AW

F



K



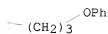
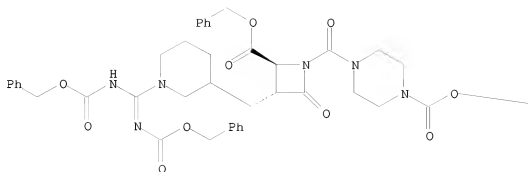
BK

3  
STEPS  
→

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BL  
YIELD 82%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F

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SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0

RGT I 144-55-8 NaHCO3

SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6

RGT N 121-44-8 Et3N

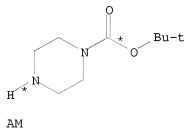
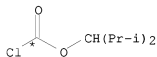
PRO BL 384830-26-6

CAT 1122-58-3 4-DMAP

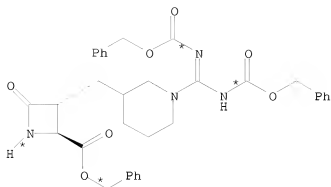
SOL 68-12-2 DMF

RX(155) OF 275 COMPOSED OF RX(29), RX(5), RX(44)

RX(155) BR + AM + AN + X ==> BC

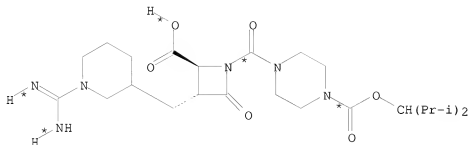


10/513699



X

3  
STEPS  
→



BC

YIELD 92%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2C12

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2C12

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(5) RCT P 253177-45-6, X 384830-18-6

RGT N 121-44-8 Et3N

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PRO Y 253177-10-5  
CAT 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

RX(44) RCT Y 253177-10-5

STAGE (1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

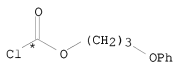
## STAGE (2)

SOL 7732-18-5 Water

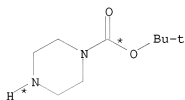
PRO BC 253177-54-7

NTE polyvinylpyridine resin used in second stage

RX(160) OF 275 COMPOSED OF RX(33), RX(25), RX(37)

$$RX(160) \quad BV + AM + AN + X \implies BZ$$


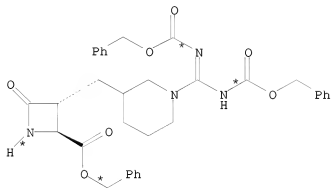
BV



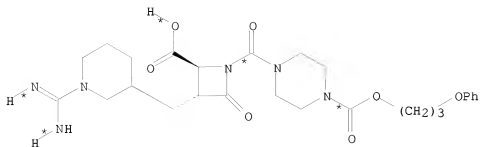
AM



AN



3  
STEPS  
→



BZ  
YIELD 92%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6  
RGT N 121-44-8 Et3N  
PRO BL 384830-26-6  
CAT 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

RX(37) RCT BL 384830-26-6

STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

STAGE(2)

SOL 7732-18-5 Water

PRO BZ 384829-80-5

NTE polyvinylpyridine resin used in second stage

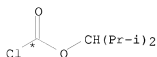
RX(168) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(4)

10/513699

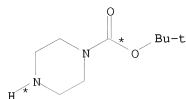
AND REACTION SEQUENCE RX(1), RX(2), RX(3), RX(4)

... BR + AM + AN ==> P...

...A + B + F + K + P ==> Q



BR

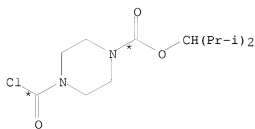


AM



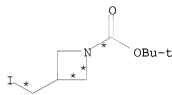
AN

4  
STEPS  
→

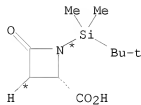


P

START NEXT REACTION SEQUENCE



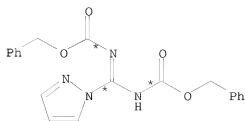
A



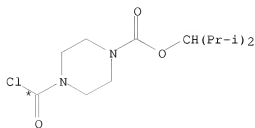
B



F



K

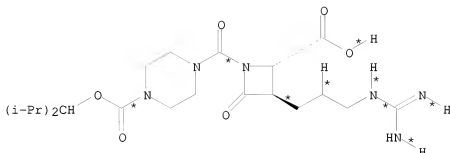


P

<12/04/2007>

Erich Leese

4  
STEPS  
→



Q

RX(29) RCT BR 30250-57-8, AM 57260-71-6

## STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

## STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

## STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(1) RCT A 253176-94-2, B 82938-50-9

RGT D 4111-54-0 LiN(Pr-i)2

PRO C 253176-95-3

SOL 109-99-9 THF

NTE stereoselective

RX(2) RCT C 253176-95-3

## STAGE(1)

RGT H 429-41-4 Bu4N.F

SOL 109-99-9 THF

## STAGE(2)

RCT F 100-39-0

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RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO G 253176-97-5

RX(3) RCT G 253176-97-5

STAGE(1)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO L 253177-00-3

NTE alternative prepn. shown

RX(4) RCT L 253177-00-3, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

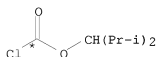
STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

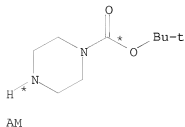
PRO Q 253173-70-5

RX(170) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(4)  
AND REACTION SEQUENCE RX(6), RX(1), RX(2), RX(3), RX(4)

... BR + AM + AN ==> P...  
...Z + B + F + K + P ==> Q



BR



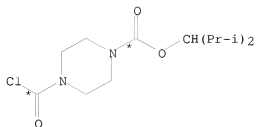
5  
STEPS  
→

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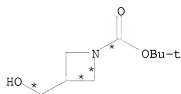


10/513699

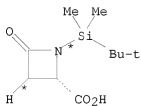


P

START NEXT REACTION SEQUENCE



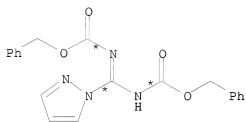
Z



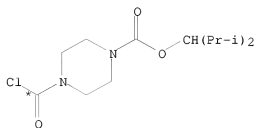
B



F



K

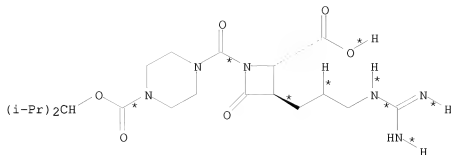


P

5  
STEPS  
→

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Q

RX(29) RCT BR 30250-57-8, AM 57260-71-6

## STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

## STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

## STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NIE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(6) RCT Z 142253-56-3

RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole

PRO A 253176-94-2

SOL 75-09-2 CH2Cl2

RX(1) RCT A 253176-94-2, B 82938-50-9

RGT D 4111-54-0 LiN(Pr-i)2

PRO C 253176-95-3

SOL 109-99-9 THF

NIE stereoselective

RX(2) RCT C 253176-95-3

## STAGE(1)

RGT H 429-41-4 Bu4N.F

SOL 109-99-9 THF

## STAGE(2)

RCT F 100-39-0

RGT I 144-55-8 NaHCO3

SOL 68-12-2 DMF

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PRO G 253176-97-5

RX(3) RCT G 253176-97-5

STAGE(1)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

PRO L 253177-00-3

NTE alternative prepn. shown

RX(4) RCT L 253177-00-3, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP

SOL 68-12-2 DMF

STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl

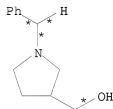
CAT 7440-05-3 Pd

SOL 123-91-1 Dioxane, 7732-18-5 Water

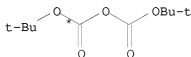
PRO Q 253173-70-5

RX(171) OF 275 COMPOSED OF RX(7), RX(8), RX(43), RX(16), RX(18)

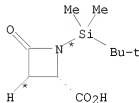
RX(171) AD + AE + B + F + K ==> BA



AD



AE

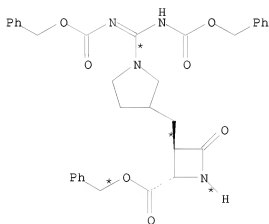
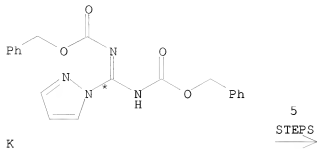


B



F

10/513699



BA

RX(7) RCT AD 5731-17-9

STAGE(1)

RGT S 1333-74-0 H2  
CAT 7440-05-3 Pd  
SOL 67-56-1 MeOH

STAGE(2)

RCT AE 24424-99-5  
SOL 109-99-9 THF

PRO AF 114214-69-6

NTE isopropanol may also be used as a solvent in the first stage

RX(8) RCT AF 114214-69-6  
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole  
PRO AH 479622-36-1  
SOL 75-09-2 CH2Cl2

RX(43) RCT AH 479622-36-1, B 82938-50-9

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RGT D 4111-54-0 LiN(Pr-i)2  
PRO AX 479622-21-4  
SOL 109-99-9 THF  
NTE stereoselective

RX(16) RCT AX 479622-21-4

STAGE(1)

RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AY 479622-22-5

RX(18) RCT AY 479622-22-5

STAGE(1)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

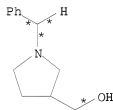
STAGE(2)

RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

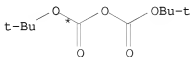
PRO BA 479622-23-6

NTE alternative prepn. shown

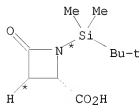
RX(173) OF 275 COMPOSED OF RX(7), RX(8), RX(43), RX(16), RX(18), RX(20)  
RX(173) AD + AE + B + F + K + P ==> BB



AD

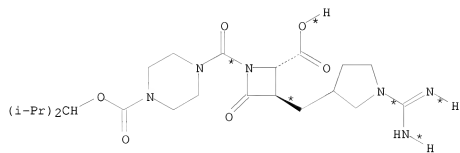
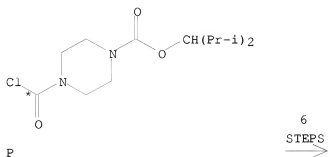
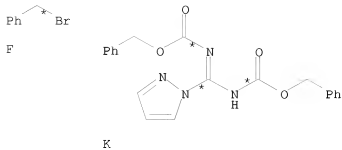


AE



B

10/513699



RX(7) RCT AD 5731-17-9

STAGE(1)

RGT S 1333-74-0 H2  
 CAT 7440-05-3 Pd  
 SOL 67-56-1 MeOH

STAGE(2)

RCT AE 24424-99-5  
 SOL 109-99-9 THF

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PRO AF 114214-69-6  
NTE isopropanol may also be used as a solvent in the first stage

RX(8) RCT AF 114214-69-6  
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole  
PRO AH 479622-36-1  
SOL 75-09-2 CH2Cl2

RX(43) RCT AH 479622-36-1, B 82938-50-9  
RGT D 4111-54-0 LiN(Pr-i)2  
PRO AX 479622-21-4  
SOL 109-99-9 THF  
NTE stereoselective

RX(16) RCT AX 479622-21-4

STAGE(1)  
RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

STAGE(2)  
RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AY 479622-22-5

RX(18) RCT AY 479622-22-5

STAGE(1)  
RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)  
RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO BA 479622-23-6  
NTE alternative prepn. shown

RX(20) RCT BA 479622-23-6, P 253177-45-6

STAGE(1)  
RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

STAGE(2)  
RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO BB 479622-24-7

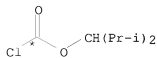
RX(201) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5)

10/513699

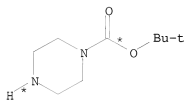
AND REACTION SEQUENCE RX(15), RX(17), RX(19), RX(5)

... BR + AM + AN ==> P...

...AL + B + F + K + P ==> Y



BR

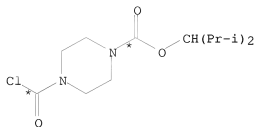


AM



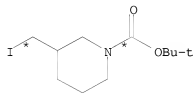
AN

4  
STEPS  
→

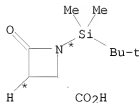


P

START NEXT REACTION SEQUENCE



AL



B



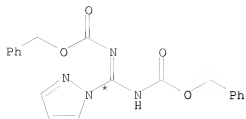
F

<12/04/2007>

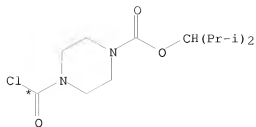
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10/513699



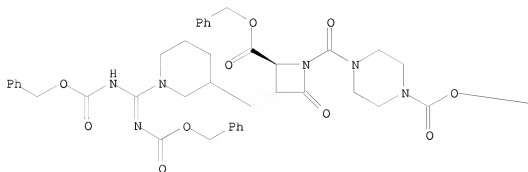
K



P

4  
STEPS  
→

PAGE 1-A



PAGE 1-B

CH(Pr-i)<sub>2</sub>

Y  
YIELD 82%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

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## STAGE(1)

RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

## STAGE(2)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

## STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(15) RCT AL 253177-03-6, B 82938-50-9  
RGT D 4111-54-0 LiN(Pr-i)2  
PRO AW 253177-04-7  
SOL 109-99-9 THF  
NTE stereoselective

RX(17) RCT AW 253177-04-7

## STAGE(1)

RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

## STAGE(2)

RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

## STAGE(1)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

## STAGE(2)

RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

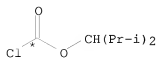
PRO X 384830-18-6

NTE alternative prepn. shown

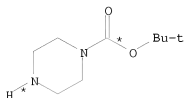
RX(5) RCT P 253177-45-6, X 384830-18-6  
RGT N 121-44-8 Et3N  
PRO Y 253177-10-5  
CAT 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

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RX(202) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(21)  
 AND REACTION SEQUENCE RX(15), RX(17), RX(19), RX(21)  
 ...4 BR + 4 AM + 4 AN ==> P...  
 ...4 AL + 4 B + 4 F + 4 K + 4 P ==> BB + BC + BD +  
 BE



4 BR

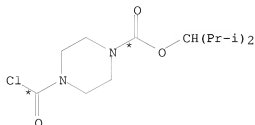


4 AM



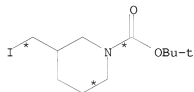
4 AN

4  
STEPS  
→

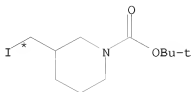


P

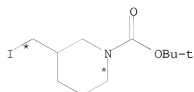
START NEXT REACTION SEQUENCE



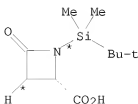
AL



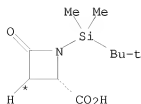
2 AL



AL



B



3 B

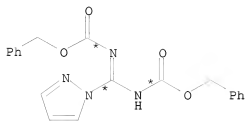
<12/04/2007>

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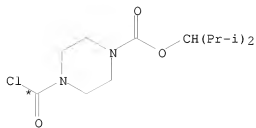
10/513699



4 F

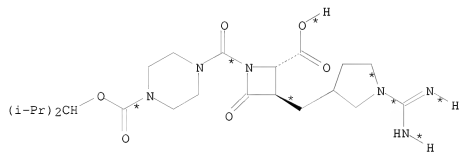


4 K

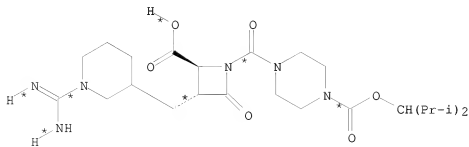


4 P

4  
STEPS  
→



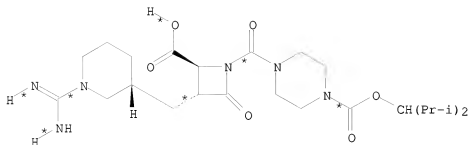
BB



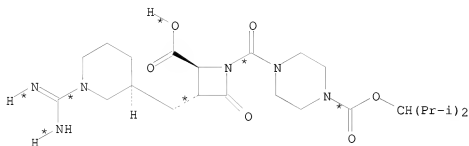
BC

<12/04/2007>

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BD



BE

RX(29) RCT BR 30250-57-8, AM 57260-71-6

## STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

## STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

## STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(15) RCT AL 253177-03-6, B 82938-50-9

RGT D 4111-54-0 LiN(Pr-i)2

PRO AW 253177-04-7

SOL 109-99-9 THF

NTE stereoselective

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RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prepn. shown

RX(21) RCT X 384830-18-6, P 253177-45-6

STAGE(1)

RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

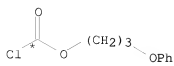
PRO BB 479622-24-7, BC 253177-54-7, BD 479622-25-8, BE  
479622-26-9

RX(206) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25)  
AND REACTION SEQUENCE RX(15), RX(17), RX(19), RX(25)

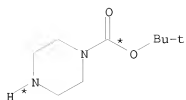
... BV + AM + AN ==> BK...

...AL + B + F + K + BK ==> BL

10/513699



BV

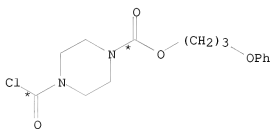


AM



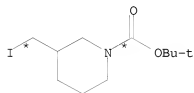
AN

4  
STEPS  
→

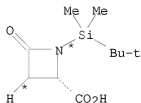


BK

START NEXT REACTION SEQUENCE



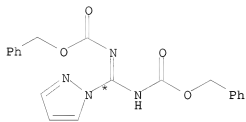
AL



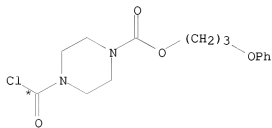
B



F



K



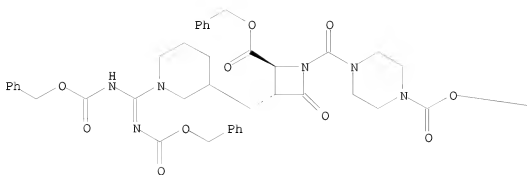
BK

<12/04/2007>

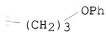
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4  
STEPS  
→

PAGE 1-A



PAGE 1-B



BL  
YIELD 82%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

## STAGE(1)

RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

## STAGE(2)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

## STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative



prepn. shown

RX(15) RCT AL 253177-03-6, B 82938-50-9  
 RGT D 4111-54-0 LiN(Pr-i)2  
 PRO AW 253177-04-7  
 SOL 109-99-9 THF  
 NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F  
 SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0  
 RGT I 144-55-8 NaHCO3  
 SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H  
 SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3  
 RGT N 121-44-8 Et3N  
 SOL 68-12-2 DMF

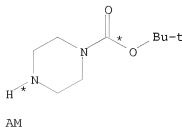
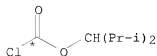
PRO X 384830-18-6

NTE alternative prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6  
 RGT N 121-44-8 Et3N  
 PRO BL 384830-26-6  
 CAT 1122-58-3 4-DMAP  
 SOL 68-12-2 DMF

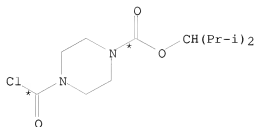
RX(214) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5)  
 AND REACTION SEQUENCE RX(10), RX(15), RX(17), RX(19), RX(5)

... BR + AM + AN ==> P...  
 ...AJ + B + F + K + P ==> Y



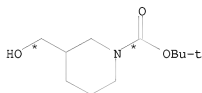
5  
 STEPS  
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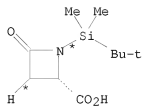


P

START NEXT REACTION SEQUENCE



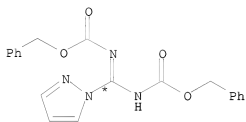
AJ



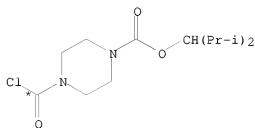
B



F



K

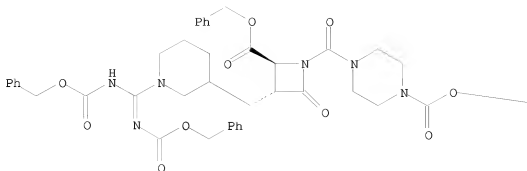


P

5  
STEPS  
→

<12/04/2007>

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$$\text{---CH(Pr-i)}_2$$

Y  
YIELD 82%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE (1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

## STAGE (2)

RGT M 76-05-1 F3CC02H

SOL 75-09-2 CH2C12

### STAGE (3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2C12

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

```
RX(10)    RCT  AJ 116574-71-1
          RGT  AA 7553-56-2 12, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole
          PRO  AL 253177-03-6
          SOL  75-09-2 CH2C12
```

RX(15) RCT AL 253177-03-6, B 82938-50-9  
 RGT D 4111-54-0 LiN(Pr-i)2  
 PRO AW 253177-04-7  
 SOL 109-99-9 THF  
 NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F  
 SOL 109-99-9 THF

STAGE(2)

RGT F 100-39-0  
 RGT I 144-55-8 NaHCO3  
 SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H  
 SOL 75-09-2 CH2Cl2

STAGE(2)

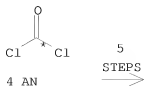
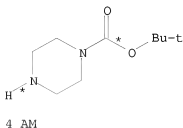
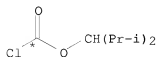
RCT K 152120-55-3  
 RGT N 121-44-8 Et3N  
 SOL 68-12-2 DMF

PRO X 384830-18-6  
 NTE alternative prepn. shown

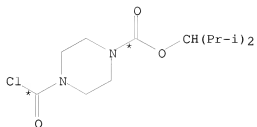
RX(5) RCT P 253177-45-6, X 384830-18-6  
 RGT N 121-44-8 Et3N  
 PRO Y 253177-10-5  
 CAT 1122-58-3 4-DMAP  
 SOL 68-12-2 DMF

RX(215) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(21)  
 AND REACTION SEQUENCE RX(10), RX(15), RX(17), RX(19), RX(21)

...4 BR + 4 AM + 4 AN ==> P...  
 ...4 AJ + 4 B + 4 F + 4 K + 4 P ==> BB + BC + BD +  
 BE

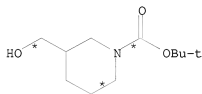


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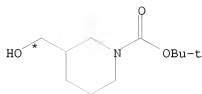


P

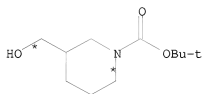
START NEXT REACTION SEQUENCE



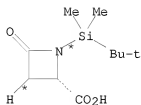
AJ



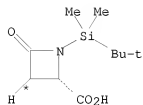
2 AJ



AJ



B



3 B

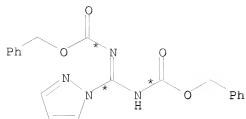


4 F

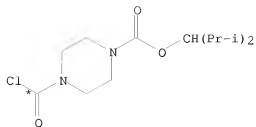
<12/04/2007>

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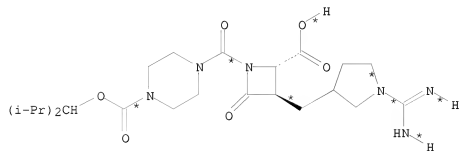


4 K

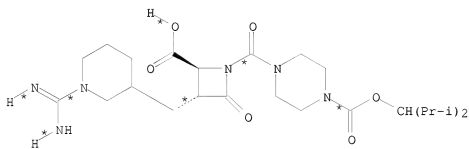


4 P

5  
STEPS  
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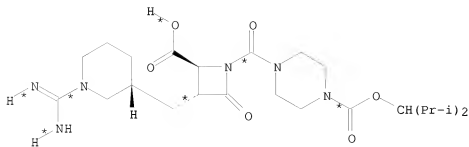
BB



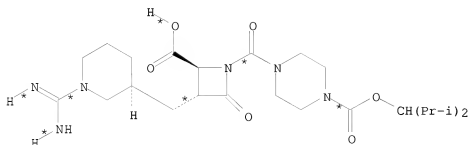
BC

<12/04/2007>

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BD



BE

RX(29) RCT BR 30250-57-8, AM 57260-71-6

## STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

## STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2C12

## STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2C12

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(10) RCT AJ 116574-71-1  
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole  
PRO AL 253177-03-6  
SOL 75-09-2 CH2C12

RX(15) RCT AL 253177-03-6, B 82938-50-9  
RGT D 4111-54-0 LiN(Pr-i)2

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PRO AW 253177-04-7  
SOL 109-99-9 THF  
NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)  
RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

STAGE(2)  
RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)  
RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)  
RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6  
NTE alternative prepn. shown

RX(21) RCT X 384830-18-6, P 253177-45-6

STAGE(1)  
RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

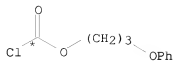
STAGE(2)  
RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO BB 479622-24-7, BC 253177-54-7, BD 479622-25-8, BE  
479622-26-9

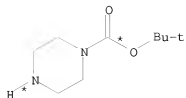
RX(219) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25)  
AND REACTION SEQUENCE RX(10), RX(15), RX(17), RX(19), RX(25)  
... BV + AM + AN ==> BK...  
...AJ + B + F + K + BK ==> BL



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BV

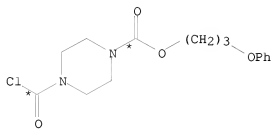


AM



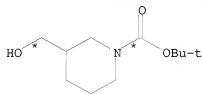
AN

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STEPS  
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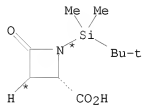


BK

START NEXT REACTION SEQUENCE



AJ

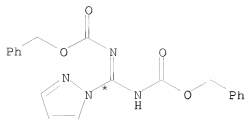


B

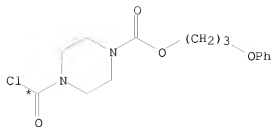


F

10/513699



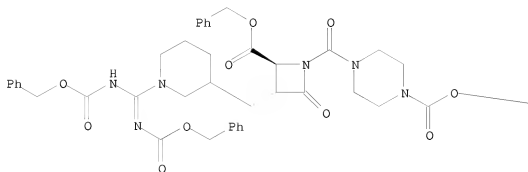
K



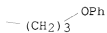
BK

5  
STEPS  
→

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PAGE 1-B



BL  
YIELD 82%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

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## STAGE(1)

RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

## STAGE(2)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

## STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(10) RCT AJ 116574-71-1  
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole  
PRO AL 253177-03-6  
SOL 75-09-2 CH2Cl2

RX(15) RCT AL 253177-03-6, B 82938-50-9  
RGT D 4111-54-0 LiN(Pr-i)2  
PRO AW 253177-04-7  
SOL 109-99-9 THF  
NTE stereoselective

RX(17) RCT AW 253177-04-7

## STAGE(1)

RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

## STAGE(2)

RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

## STAGE(1)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

## STAGE(2)

RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prep. shown

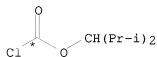
RX(25) RCT BK 479622-28-1, X 384830-18-6  
RGT N 121-44-8 Et3N

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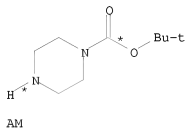
PRO BL 384830-26-6  
CAT 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

RX(227) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5)  
AND REACTION SEQUENCE RX(9), RX(10), RX(15), RX(17), RX(19),  
RX(5)

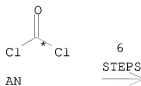
... BR + AM + AN ==> P...  
... AI + AE + B + F + K + P ==> Y



BR

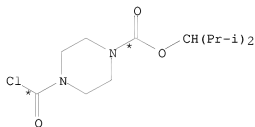


AM



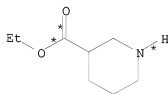
AN

6  
STEPS  
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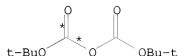


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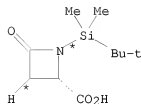
START NEXT REACTION SEQUENCE



AI

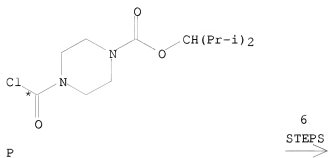
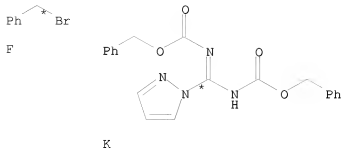


AE

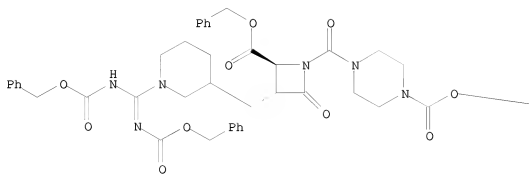


B

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PAGE 1-A



—CH(Pr-i)<sub>2</sub>

Y  
YIELD 82%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et<sub>3</sub>N  
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F<sub>3</sub>CCO<sub>2</sub>H  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et<sub>3</sub>N  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(9) RCT AI 5006-62-2, AE 24424-99-5

STAGE(1)

SOL 109-99-9 THF

STAGE(2)

RGT AK 16853-85-3 LiAlH<sub>4</sub>  
SOL 109-99-9 THF

PRO AJ 116574-71-1

RX(10) RCT AJ 116574-71-1  
RGT AA 7553-56-2 I<sub>2</sub>, AB 603-35-0 PPh<sub>3</sub>, AC 288-32-4 1H-Imidazole  
PRO AL 253177-03-6  
SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

RX(15) RCT AL 253177-03-6, B 82938-50-9  
RGT D 4111-54-0 LiN(Pr-i)<sub>2</sub>  
PRO AW 253177-04-7  
SOL 109-99-9 THF  
NTE stereoselective

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RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)

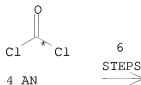
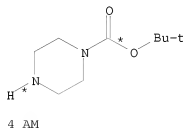
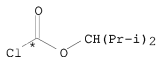
RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6  
NTE alternative prepn. shown

RX(5) RCT P 253177-45-6, X 384830-18-6  
RGT N 121-44-8 Et3N  
PRO Y 253177-10-5  
CAT 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

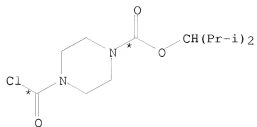
RX(228) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(21)  
AND REACTION SEQUENCE RX(9), RX(10), RX(15), RX(17), RX(19),  
RX(21)

...4 BR + 4 AM + 4 AN ==> P...  
...4 AI + 4 AE + 4 B + 4 F + 4 K + 4 P ==> BB + BC +  
BD + BE



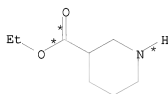
6  
STEPS  
→

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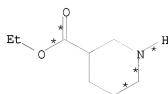


P

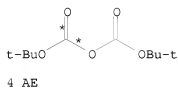
START NEXT REACTION SEQUENCE



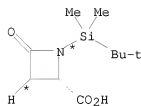
3 AI



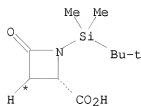
AI



4 AE



B



3 B



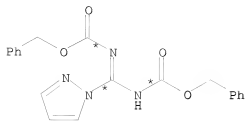
4 F

<12/04/2007>

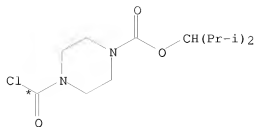
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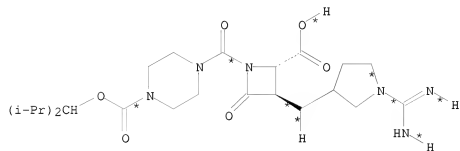


4 K

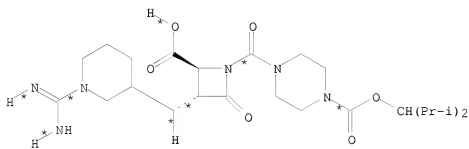


4 P

6  
STEPS  
→



BB

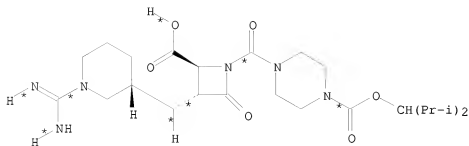


BC

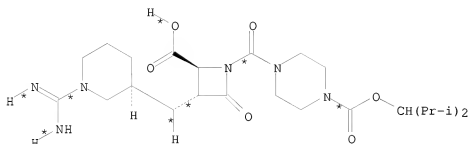
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BD



BE

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(9) RCT AI 5006-62-2, AE 24424-99-5

STAGE(1)

SOL 109-99-9 THF

STAGE(2)

RGT AK 16853-85-3 LiAlH4

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SOL 109-99-9 THF

PRO AJ 116574-71-1

RX(10) RCT AJ 116574-71-1  
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole  
PRO AL 253177-03-6  
SOL 75-09-2 CH2Cl2

RX(15) RCT AL 253177-03-6, B 82938-50-9  
RGT D 4111-54-0 LiN(Pr-i)2  
PRO AW 253177-04-7  
SOL 109-99-9 THF  
NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)  
RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

STAGE(2)  
RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)  
RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)  
RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6  
NTE alternative prepn. shown

RX(21) RCT X 384830-18-6, P 253177-45-6

STAGE(1)  
RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

STAGE(2)  
RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

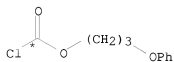
PRO BB 479622-24-7, BC 253177-54-7, BD 479622-25-8, BE 479622-26-9

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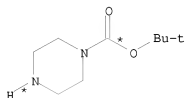
RX(232) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25)  
AND REACTION SEQUENCE RX(9), RX(10), RX(15), RX(17), RX(19),  
RX(25)

... BV + AM + AN ==> BK...

...AI + AE + B + F + K + BK ==> BL



BV

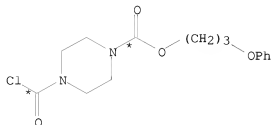


AM



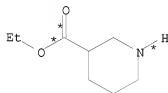
AN

6  
STEPS  
=>

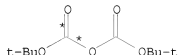


BK

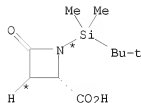
START NEXT REACTION SEQUENCE



AI



AE

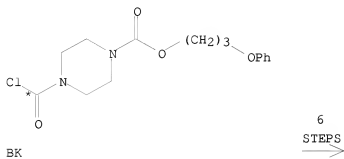
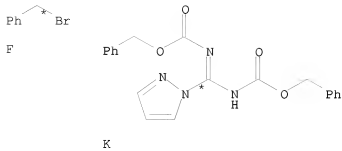


B

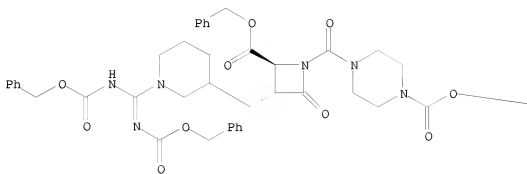
<12/04/2007>

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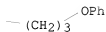


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BL  
YIELD 82%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(9) RCT AI 5006-62-2, AE 24424-99-5

STAGE(1)

SOL 109-99-9 THF

STAGE(2)

RGT AK 16853-85-3 LiAlH4  
SOL 109-99-9 THF

PRO AJ 116574-71-1

RX(10) RCT AJ 116574-71-1  
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole  
PRO AL 253177-03-6  
SOL 75-09-2 CH2Cl2

RX(15) RCT AL 253177-03-6, B 82938-50-9  
RGT D 4111-54-0 LiN(Pr-i)2  
PRO AW 253177-04-7  
SOL 109-99-9 THF  
NTE stereoselective

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RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6

RGT N 121-44-8 Et3N

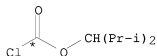
PRO BL 384830-26-6

CAT 1122-58-3 4-DMAP

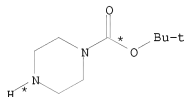
SOL 68-12-2 DMF

RX(233) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(20)  
AND REACTION SEQUENCE RX(43), RX(16), RX(18), RX(20)

... BR + AM + AN ==> P...  
...AH + B + F + K + P ==> BB



BR



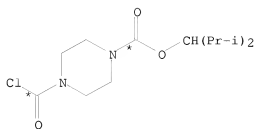
AM



AN

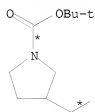
4  
STEPS  
→

10/513699

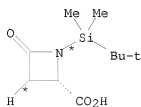


P

START NEXT REACTION SEQUENCE



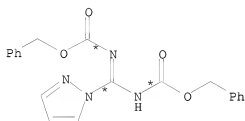
AH



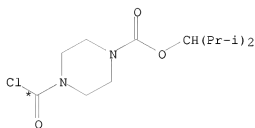
B



F

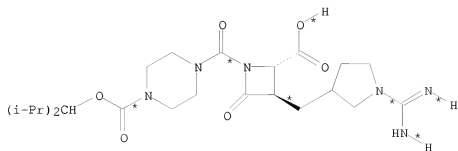


K



P

4  
STEPS  
→



BB

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RX(29) RCT BR 30250-57-8, AM 57260-71-6

## STAGE(1)

RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

## STAGE(2)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

## STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(43) RCT AH 479622-36-1, B 82938-50-9

RGT D 4111-54-0 LiN(Pr-i)2

PRO AX 479622-21-4

SOL 109-99-9 THF

NTE stereoselective

RX(16) RCT AX 479622-21-4

## STAGE(1)

RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

## STAGE(2)

RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AY 479622-22-5

RX(18) RCT AY 479622-22-5

## STAGE(1)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

## STAGE(2)

RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO BA 479622-23-6

NTE alternative prep. shown

RX(20) RCT BA 479622-23-6, P 253177-45-6

## STAGE(1)

10/513699

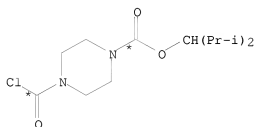
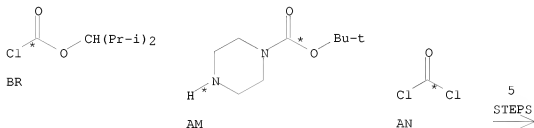
RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

STAGE(2)

RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

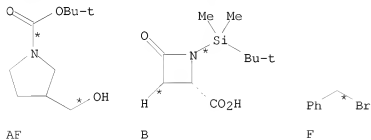
PRO BB 479622-24-7

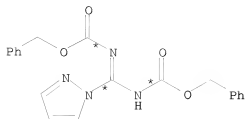
RX(234) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(20)  
AND REACTION SEQUENCE RX(8), RX(43), RX(16), RX(18), RX(20)  
... BR + AM + AN ==> P...  
...AF + B + F + K + P ==> BB



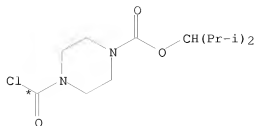
P

START NEXT REACTION SEQUENCE



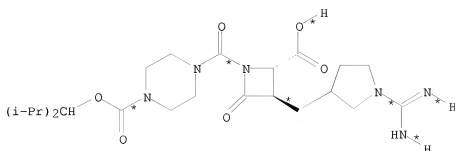


K



P

5  
STEPS  
→



BB

RX(29) RCT BR 30250-57-8, AM 57260-71-6

## STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

## STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

## STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative prepn. shown

RX(8) RCT AF 114214-69-6  
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole  
PRO AH 479622-36-1  
SOL 75-09-2 CH2Cl2

RX(43) RCT AH 479622-36-1, B 82938-50-9

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RGT D 4111-54-0 LiN(Pr-i)2  
PRO AX 479622-21-4  
SOL 109-99-9 THF  
NTE stereoselective

RX(16) RCT AX 479622-21-4

STAGE(1)  
RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

STAGE(2)  
RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AY 479622-22-5

RX(18) RCT AY 479622-22-5

STAGE(1)  
RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)  
RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO BA 479622-23-6  
NTE alternative prepn. shown

RX(20) RCT BA 479622-23-6, P 253177-45-6

STAGE(1)  
RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

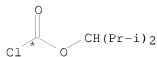
STAGE(2)  
RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

PRO BB 479622-24-7

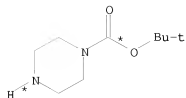
RX(235) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(20)  
AND REACTION SEQUENCE RX(7), RX(8), RX(43), RX(16), RX(18),  
RX(20)

... BR + AM + AN ==> P...  
...AD + AE + B + F + K + P ==> BB

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BR

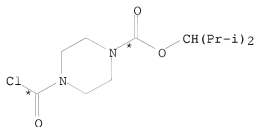


AM



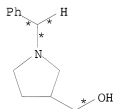
AN

6  
STEPS  
➡

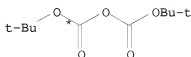


P

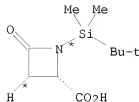
START NEXT REACTION SEQUENCE



AD



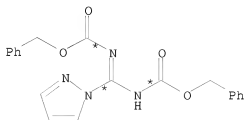
AE



B



F



K

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STAGE(2)  
RCT AE 24424-99-5  
SOL 109-99-9 THF

PRO AF 114214-69-6  
NTE isopropanol may also be used as a solvent in the first stage

RX(8) RCT AF 114214-69-6  
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole  
PRO AH 479622-36-1  
SOL 75-09-2 CH2Cl2

RX(43) RCT AH 479622-36-1, B 82938-50-9  
RGT D 4111-54-0 LiN(Pr-i)2  
PRO AX 479622-21-4  
SOL 109-99-9 THF  
NTE stereoselective

RX(16) RCT AX 479622-21-4

STAGE(1)  
RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

STAGE(2)  
RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AY 479622-22-5

RX(18) RCT AY 479622-22-5

STAGE(1)  
RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)  
RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO BA 479622-23-6  
NTE alternative prepn. shown

RX(20) RCT BA 479622-23-6, P 253177-45-6

STAGE(1)  
RGT N 121-44-8 Et3N, R 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

STAGE(2)  
RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

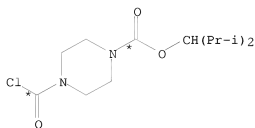
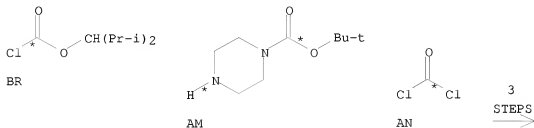
10/513699

PRO BB 479622-24-7

RX(241) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5), RX(44)  
AND REACTION SEQUENCE RX(19), RX(5), RX(44)

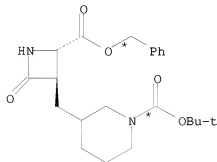
... BR + AM + AN ==> P...

...AZ + K + P ==> BC

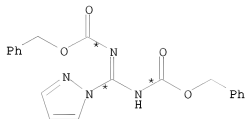


P

START NEXT REACTION SEQUENCE



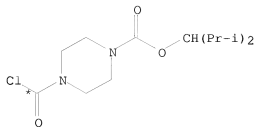
AZ



K

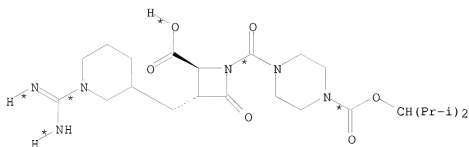


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P

3  
STEPS  
→



BC

YIELD 92%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

<12/04/2007>

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## STAGE(2)

RCT K 152120-55-3  
 RGT N 121-44-8 Et3N  
 SOL 68-12-2 DMF

PRO X 384830-18-6  
 NTE alternative prepn. shown

RX(5) RCT P 253177-45-6, X 384830-18-6  
 RGT N 121-44-8 Et3N  
 PRO Y 253177-10-5  
 CAT 1122-58-3 4-DMAP  
 SOL 68-12-2 DMF

RX(44) RCT Y 253177-10-5

## STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl  
 CAT 7440-05-3 Pd  
 SOL 123-91-1 Dioxane, 7732-18-5 Water

## STAGE(2)

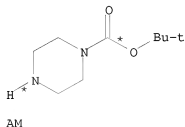
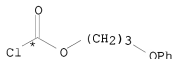
SOL 7732-18-5 Water

PRO BC 253177-54-7  
 NTE polyvinylpyridine resin used in second stage

RX(245) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25), RX(37)  
 AND REACTION SEQUENCE RX(19), RX(25), RX(37)

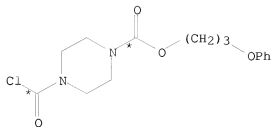
... BV + AM + AN ==> BK...

...AZ + K + BK ==> BZ



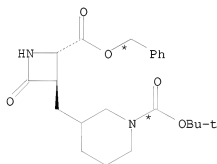
3  
 STEPS  
 →

10/513699

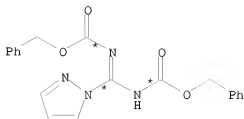


BK

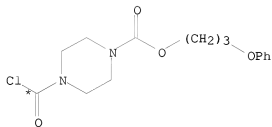
START NEXT REACTION SEQUENCE



AZ



K

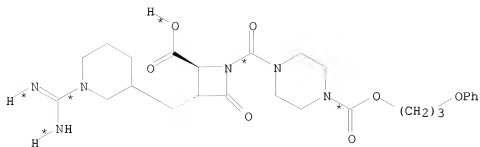


BK

3  
STEPS  
→

<12/04/2007>

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BZ  
YIELD 92%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6

RGT N 121-44-8 Et3N  
PRO BL 384830-26-6  
CAT 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

RX(37) RCT BL 384830-26-6

## STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl

CAT 7440-05-3 Pd

SOL 123-91-1 Dioxane, 7732-18-5 Water

## STAGE(2)

SOL 7732-18-5 Water

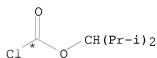
PRO BZ 384829-80-5

NTE polyvinylpyridine resin used in second stage

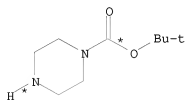
RX(248) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5), RX(44)  
AND REACTION SEQUENCE RX(17), RX(19), RX(5), RX(44)

... BR + AM + AN ==&gt; P...

...AW + F + K + P ==&gt; BC



BR

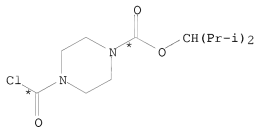


AM



AN

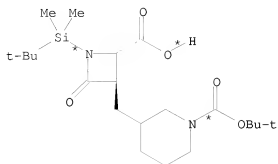
4  
STEPS  
→



P

START NEXT REACTION SEQUENCE

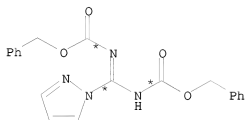
10/513699



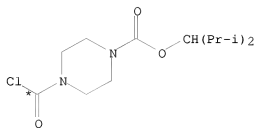
AW



F

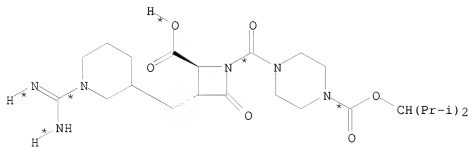


K



P

4  
STEPS  
→



BC  
YIELD 92%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

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STAGE(1)  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

STAGE(2)  
RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(3)  
RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO P 253177-45-6  
NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(17) RCT AW 253177-04-7

STAGE(1)  
RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

STAGE(2)  
RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)  
RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)  
RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6  
NTE alternative prepn. shown

RX(5) RCT P 253177-45-6, X 384830-18-6  
RGT N 121-44-8 Et3N  
PRO Y 253177-10-5  
CAT 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

RX(44) RCT Y 253177-10-5

STAGE(1)  
RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

10/513699

STAGE(2)

SOL 7732-18-5 Water

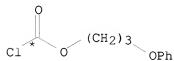
PRO BC 253177-54-7

NTE polyvinylpyridine resin used in second stage

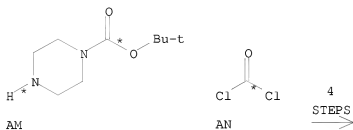
RX(252) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25), RX(37)  
AND REACTION SEQUENCE RX(17), RX(19), RX(25), RX(37)

... BV + AM + AN ==> BK...

...AM + F + K + BK ==> BZ



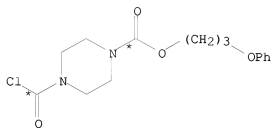
BV



AM

AN

4  
STEPS  
→

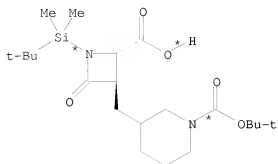


BK

START NEXT REACTION SEQUENCE



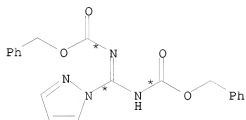
10/513699



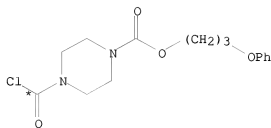
AW



F

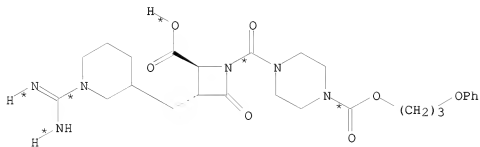


K



BK

4  
STEPS  
→



BZ  
YIELD 92%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

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STAGE(1)  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

STAGE(2)  
RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(3)  
RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1  
NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(17) RCT AW 253177-04-7

STAGE(1)  
RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

STAGE(2)  
RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)  
RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)  
RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6  
NTE alternative prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6  
RGT N 121-44-8 Et3N  
PRO BL 384830-26-6  
CAT 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

RX(37) RCT BL 384830-26-6

STAGE(1)  
RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

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STAGE(2)

SOL 7732-18-5 Water

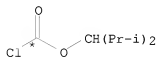
PRO BZ 384829-80-5

NTE polyvinylpyridine resin used in second stage

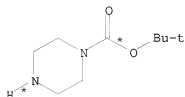
RX(255) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5), RX(44)  
AND REACTION SEQUENCE RX(15), RX(17), RX(19), RX(5), RX(44)

... BR + AM + AN ==> P...

...AL + B + F + K + P ==> BC



BR

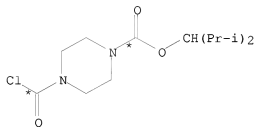


AM



AN

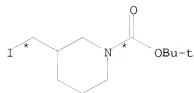
5  
STEPS  
→



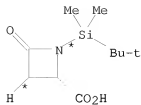
P

START NEXT REACTION SEQUENCE

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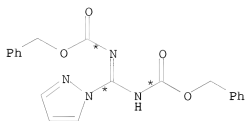
AL



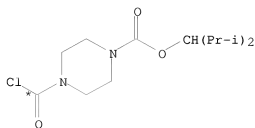
B



F

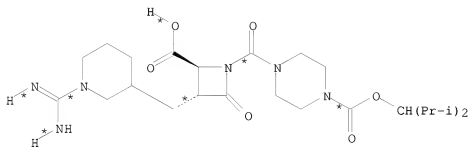


K



P

5  
STEPS  
→



BC  
YIELD 92%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

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## STAGE(2)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

## STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(15) RCT AL 253177-03-6, B 82938-50-9  
RGT D 4111-54-0 LiN(Pr-i)2  
PRO AW 253177-04-7  
SOL 109-99-9 THF  
NTE stereoselective

RX(17) RCT AW 253177-04-7

## STAGE(1)

RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

## STAGE(2)

RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

## STAGE(1)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

## STAGE(2)

RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prep. shown

RX(5) RCT P 253177-45-6, X 384830-18-6  
RGT N 121-44-8 Et3N  
PRO Y 253177-10-5  
CAT 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

RX(44) RCT Y 253177-10-5

## STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd

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SOL 123-91-1 Dioxane, 7732-18-5 Water

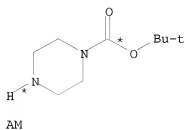
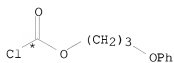
STAGE(2)

SOL 7732-18-5 Water

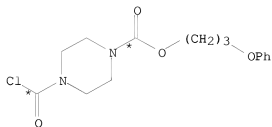
PRO BC 253177-54-7

NTE polyvinylpyridine resin used in second stage

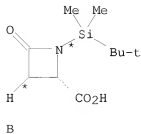
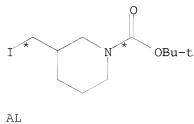
RX(259) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25), RX(37)  
AND REACTION SEQUENCE RX(15), RX(17), RX(19), RX(25), RX(37)  
... BV + AM + AN ==> BK...  
...AL + B + F + K + BK ==> BZ



5  
STEPS  
→



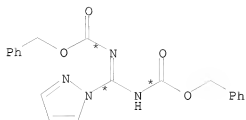
START NEXT REACTION SEQUENCE



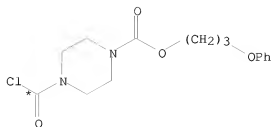
<12/04/2007>

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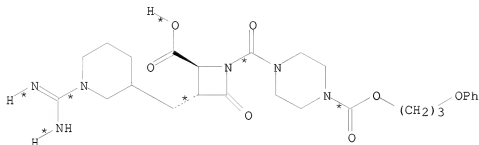


K



BK

5  
STEPS  
→



BZ  
YIELD 92%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative

<12/04/2007>

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prepn. shown

RX(15) RCT AL 253177-03-6, B 82938-50-9  
 RGT D 4111-54-0 LiN(Pr-i)2  
 PRO AW 253177-04-7  
 SOL 109-99-9 THF  
 NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F  
 SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0  
 RGT I 144-55-8 NaHCO3  
 SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H  
 SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3  
 RGT N 121-44-8 Et3N  
 SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6  
 RGT N 121-44-8 Et3N  
 PRO BL 384830-26-6  
 CAT 1122-58-3 4-DMAP  
 SOL 68-12-2 DMF

RX(37) RCT BL 384830-26-6

STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl  
 CAT 7440-05-3 Pd  
 SOL 123-91-1 Dioxane, 7732-18-5 Water

STAGE(2)

SOL 7732-18-5 Water

PRO BZ 384829-80-5

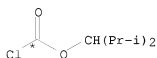
NTE polyvinylpyridine resin used in second stage

RX(262) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5), RX(44)  
 AND REACTION SEQUENCE RX(10), RX(15), RX(17), RX(19), RX(5),

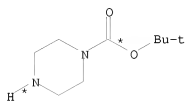


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RX(44)  
 ... BR + AM + AN ==> P...  
 ...AJ + B + F + K + P ==> BC



BR

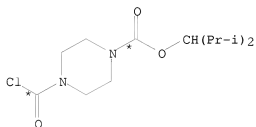


AM



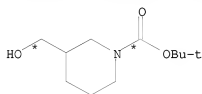
AN

6  
STEPS

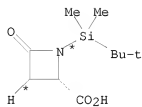


P

START NEXT REACTION SEQUENCE



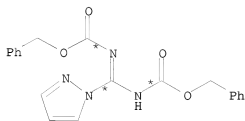
AJ



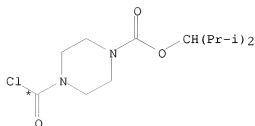
B



F



K



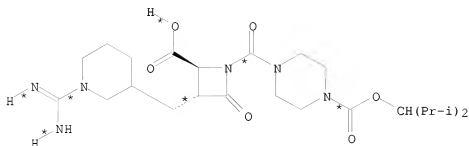
P

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6  
STEPS  
→



BC  
YIELD 92%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO P 253177-45-6

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(10) RCT AJ 116574-71-1  
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole  
PRO AL 253177-03-6  
SOL 75-09-2 CH2Cl2

RX(15) RCT AL 253177-03-6, B 82938-50-9  
RGT D 4111-54-0 LiN(Pr-i)2  
PRO AW 253177-04-7  
SOL 109-99-9 THF  
NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)

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RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prepn. shown

RX(5) RCT P 253177-45-6, X 384830-18-6

RGT N 121-44-8 Et3N

PRO Y 253177-10-5

CAT 1122-58-3 4-DMAP

SOL 68-12-2 DMF

RX(44) RCT Y 253177-10-5

STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

STAGE(2)

SOL 7732-18-5 Water

PRO BC 253177-54-7

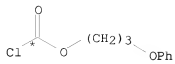
NTE polyvinylpyridine resin used in second stage

RX(266) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25), RX(37)  
AND REACTION SEQUENCE RX(10), RX(15), RX(17), RX(19), RX(25),  
RX(37)

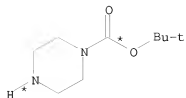
... BV + AM + AN ==> BK...

...AJ + B + F + K + BK ==> BZ

10/513699



BV

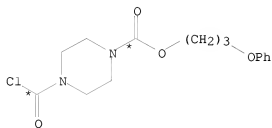


AM



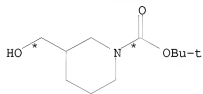
AN

6  
STEPS  
→

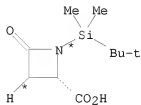


BK

START NEXT REACTION SEQUENCE



AJ

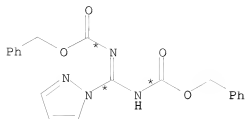


B

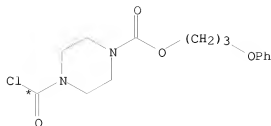


F

10/513699

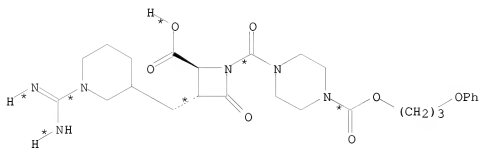


K



BK

6  
STEPS  
→



BZ

YIELD 92%

RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et<sub>3</sub>N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F<sub>3</sub>CCO<sub>2</sub>H

SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et<sub>3</sub>N

SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

<12/04/2007>

Erich Leese

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RX(10) RCT AJ 116574-71-1  
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole  
PRO AL 253177-03-6  
SOL 75-09-2 CH2Cl2

RX(15) RCT AL 253177-03-6, B 82938-50-9  
RGT D 4111-54-0 LiN(Pr-i)2  
PRO AW 253177-04-7  
SOL 109-99-9 THF  
NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6

NTE alternative prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6  
RGT N 121-44-8 Et3N  
PRO BL 384830-26-6  
CAT 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

RX(37) RCT BL 384830-26-6

STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

STAGE(2)

SOL 7732-18-5 Water

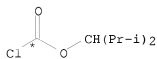
PRO BZ 384829-80-5

NTE polyvinylpyridine resin used in second stage

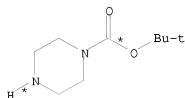
10/513699

RX(271) OF 275 COMPOSED OF REACTION SEQUENCE RX(29), RX(5), RX(44)  
AND REACTION SEQUENCE RX(9), RX(10), RX(15), RX(17), RX(19),  
RX(5), RX(44)

... BR + AM + AN ==> P...  
...AI + AE + B + F + K + P ==> BC



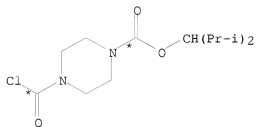
BR



AM

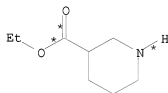


AN

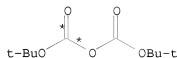


P

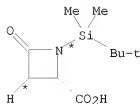
START NEXT REACTION SEQUENCE



AI

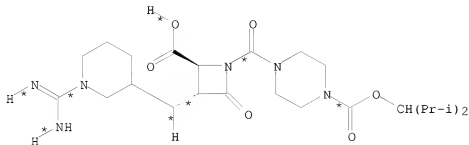
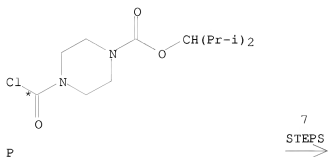
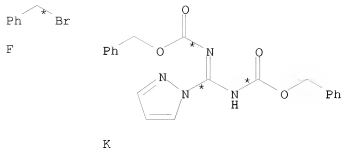


AE



B

10/513699



YIELD 92%

RX(29) RCT BR 30250-57-8, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et<sub>3</sub>N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F<sub>3</sub>CCO<sub>2</sub>H

SOL 75-09-2 CH<sub>2</sub>Cl<sub>2</sub>

STAGE(3)

<12/04/2007>

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RCT AN 75-44-5  
RGT N 121-44-8 Et3N  
SOL 75-09-2 CH2Cl2

PRO P 253177-45-6  
NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(9) RCT AI 5006-62-2, AE 24424-99-5

STAGE(1)  
SOL 109-99-9 THF

STAGE(2)  
RGT AK 16853-85-3 LiAlH4  
SOL 109-99-9 THF

PRO AJ 116574-71-1

RX(10) RCT AJ 116574-71-1  
RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole  
PRO AL 253177-03-6  
SOL 75-09-2 CH2Cl2

RX(15) RCT AL 253177-03-6, B 82938-50-9  
RGT D 4111-54-0 LiN(Pr-i)2  
PRO AW 253177-04-7  
SOL 109-99-9 THF  
NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)  
RGT H 429-41-4 Bu4N.F  
SOL 109-99-9 THF

STAGE(2)  
RCT F 100-39-0  
RGT I 144-55-8 NaHCO3  
SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)  
RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)  
RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6  
NTE alternative prepn. shown

10/513699

RX(5) RCT P 253177-45-6, X 384830-18-6  
RGT N 121-44-8 Et3N  
PRO Y 253177-10-5  
CAT 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

RX(44) RCT Y 253177-10-5

STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

STAGE(2)

SOL 7732-18-5 Water

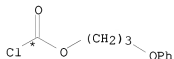
PRO BC 253177-54-7

NTE polyvinylpyridine resin used in second stage

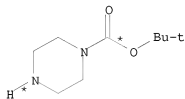
RX(275) OF 275 COMPOSED OF REACTION SEQUENCE RX(33), RX(25), RX(37)  
AND REACTION SEQUENCE RX(9), RX(10), RX(15), RX(17), RX(19),  
RX(25), RX(37)

... BV + AM + AN ==> BK...

...AI + AE + B + F + K + BK ==> BZ



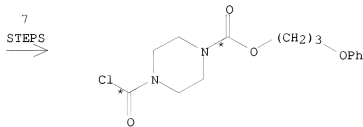
BV



AM



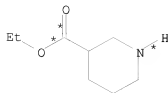
AN



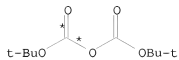
BK

START NEXT REACTION SEQUENCE

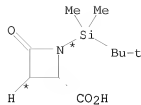
10/513699



AI



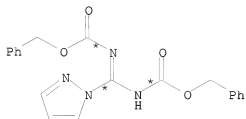
AE



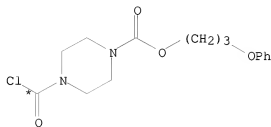
B



F

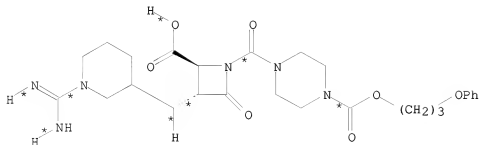


K



BK

7  
STEPS  
→



BZ  
YIELD 92%

<12/04/2007>

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RX(33) RCT BV 27184-60-7, AM 57260-71-6

STAGE(1)

RGT N 121-44-8 Et3N

SOL 68-12-2 DMF

STAGE(2)

RGT M 76-05-1 F3CCO2H

SOL 75-09-2 CH2Cl2

STAGE(3)

RCT AN 75-44-5

RGT N 121-44-8 Et3N

SOL 75-09-2 CH2Cl2

PRO BK 479622-28-1

NTE sodium bicarbonate may also be used in stage 3, alternative  
prepn. shown

RX(9) RCT AI 5006-62-2, AE 24424-99-5

STAGE(1)

SOL 109-99-9 THF

STAGE(2)

RGT AK 16853-85-3 LiAlH4

SOL 109-99-9 THF

PRO AJ 116574-71-1

RX(10) RCT AJ 116574-71-1

RGT AA 7553-56-2 I2, AB 603-35-0 PPh3, AC 288-32-4 1H-Imidazole

PRO AL 253177-03-6

SOL 75-09-2 CH2Cl2

RX(15) RCT AL 253177-03-6, B 82938-50-9

RGT D 4111-54-0 LiN(Pr-i)2

PRO AW 253177-04-7

SOL 109-99-9 THF

NTE stereoselective

RX(17) RCT AW 253177-04-7

STAGE(1)

RGT H 429-41-4 Bu4N.F

SOL 109-99-9 THF

STAGE(2)

RCT F 100-39-0

RGT I 144-55-8 NaHCO3

SOL 68-12-2 DMF

PRO AZ 253177-06-9

RX(19) RCT AZ 253177-06-9

STAGE(1)

RGT M 76-05-1 F3CCO2H  
SOL 75-09-2 CH2Cl2

STAGE(2)

RCT K 152120-55-3  
RGT N 121-44-8 Et3N  
SOL 68-12-2 DMF

PRO X 384830-18-6  
NTE alternative prepn. shown

RX(25) RCT BK 479622-28-1, X 384830-18-6  
RGT N 121-44-8 Et3N  
PRO BL 384830-26-6  
CAT 1122-58-3 4-DMAP  
SOL 68-12-2 DMF

RX(37) RCT BL 384830-26-6

STAGE(1)

RGT S 1333-74-0 H2, T 7647-01-0 HCl  
CAT 7440-05-3 Pd  
SOL 123-91-1 Dioxane, 7732-18-5 Water

STAGE(2)

SOL 7732-18-5 Water

PRO BZ 384829-80-5

NTE polyvinylpyridine resin used in second stage

SO Bioorganic & Medicinal Chemistry Letters (2002), 12(21),  
3235-3238

CODEN: BMCLE8; ISSN: 0960-894X

=&gt; d ih

'IH' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

The following are valid formats:

ABS ----- GI and AB  
 ALL ----- BIB, AB, IND, RE, Single-step Reactions  
 APPS ----- AI, PRAI  
 BIB ----- AN, plus Bibliographic Data  
 CAN ----- List of CA abstract numbers without answer numbers  
 CBIB ----- AN, plus Compressed Bibliographic Data  
 DALL ----- ALL, delimited (end of each field identified)  
 IABS ----- ABS, indented with text labels  
 IALL ----- ALL, indented with text labels  
 IBIB ----- BIB, indented with text labels  
 IND ----- Indexing data  
 IPC ----- International Patent Classifications  
 ISTD ----- STD, indented with text labels  
 OBIB ----- AN, plus Bibliographic Data (original)  
 OIBIB ----- OBIB, indented with text labels  
  
 SBIB ----- BIB, no citations  
 SIBIB ----- IBIB, no citations  
  
 MAX ----- Same as ALL  
 PATS ----- PI, SO  
 SCAN ----- TI and FCRD (random display, no answer number. SCAN  
 must be entered on the same line as DISPLAY, e.g.,  
 D SCAN.)  
 SSRX ----- Single-Step Reactions (Map, Diagram, and Summary for  
 all single-step reactions)  
 STD ----- BIB, IPC, and NCL  
  
 CRD ----- Compact Display of All Hit Reactions  
 CRDREF ----- Compact Reaction Display and SO, PY for Reference  
 FHIT ----- Reaction Map, Diagram, and Summary for first  
 hit reaction  
 FHITCBIB --- FHIT, AN plus CBIB  
 FCRD ----- First hit in Compact Reaction Display (CRD) format  
 FCRDREF ---- First hit in Compact Reaction Display (CRD) format with  
 CA reference information (SO, PY). (Default)  
 FPATH ----- PATH, plus Reaction Summary for the "long path"  
 FSPATH ----- SPATH, plus Reaction Summary for the "short path"  
 HIT ----- Reaction Map, Reaction Diagram, and Reaction  
 Summary for all hit reactions and fields containing  
 hit terms  
 OCC ----- All hit fields and the number of occurrences of the  
 hit terms in each field. Includes total number of  
 HIT, PATH, SPATH reactions. Labels reactions that have  
 incomplete verifications.  
 PATH ----- Reaction Map and Reaction Diagram for the "long  
 path". Displays all hit reactions, except those  
 whose steps are totally included within another hit  
 reaction which is displayed  
 RX ----- Hit Reactions (Map, Diagram, Summary for all hit reactions)  
 RXG ----- Hit Reaction Graphics (Map and Diagram for all hit reactions)

RXL ----- Hit Reaction Long (Map, Diagram, Summary for all hit reactions)  
 RXS ----- Hit Reaction Summaries (Map and Summary for all hit reactions)  
 SPATH ----- Reaction Map and Reaction Diagram for the "short path". Displays all single step reactions which contain a hit substance. Also displays those multistep reactions that have a hit substance in both the first and last steps of the reaction, except for those hit reactions whose steps are totally included within another hit reaction which is displayed

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of combinations include: D TI; D BIB RX; D TI, AU, FCRD. The information is displayed in the same order as the specification. All of the formats, except CRD, CRDREF, FHIT, PATH, FPATH, SPATH, FSPATH, FCRD, FCRDREF, HIT, RX, RXG, RXS, SCAN, and OCC, may be used with the DISPLAY command to display the record for a specified Accession Number.

ENTER DISPLAY FORMAT (FCRDREF):d his  
 'D' IS NOT A VALID FORMAT FOR FILE 'CASREACT'

The following are valid formats:

ABS ----- GI and AB  
 ALL ----- BIB, AB, IND, RE, Single-step Reactions  
 APPS ----- AI, PRAI  
 BIB ----- AN, plus Bibliographic Data  
 CAN ----- List of CA abstract numbers without answer numbers  
 CBIB ----- AN, plus Compressed Bibliographic Data  
 DALL ----- ALL, delimited (end of each field identified)  
 IABS ----- ABS, indented with text labels  
 IALL ----- ALL, indented with text labels  
 IBIB ----- BIB, indented with text labels  
 IND ----- Indexing data  
 IPC ----- International Patent Classifications  
 ISTD ----- STD, indented with text labels  
 OBIB ----- AN, plus Bibliographic Data (original)  
 OIBIB ----- OIBIB, indented with text labels  
  
 SBIB ----- BIB, no citations  
 SIBIB ----- IBIB, no citations  
  
 MAX ----- Same as ALL  
 PATS ----- PI, SO  
 SCAN ----- TI and FCRD (random display, no answer number. SCAN must be entered on the same line as DISPLAY, e.g., D SCAN.)  
 SSRX ----- Single-Step Reactions (Map, Diagram, and Summary for all single-step reactions)  
 STD ----- BIB, IPC, and NCL  
  
 CRD ----- Compact Display of All Hit Reactions  
 CRDREF ----- Compact Reaction Display and SO, PY for Reference  
 FHIT ----- Reaction Map, Diagram, and Summary for first hit reaction  
 FHITCBIB --- FHIT, AN plus CBIB

FCRD ----- First hit in Compact Reaction Display (CRD) format  
 FCRDREF ---- First hit in Compact Reaction Display (CRD) format with  
                   CA reference information (SO, PY). (Default)  
 FPATH ----- PATH, plus Reaction Summary for the "long path"  
 FSPATH ----- SPATH, plus Reaction Summary for the "short path"  
 HIT ----- Reaction Map, Reaction Diagram, and Reaction  
                   Summary for all hit reactions and fields containing  
                   hit terms  
 OCC ----- All hit fields and the number of occurrences of the  
                   hit terms in each field. Includes total number of  
                   HIT, PATH, SPATH reactions. Labels reactions that have  
                   incomplete verifications.  
 PATH ----- Reaction Map and Reaction Diagram for the "long  
                   path". Displays all hit reactions, except those  
                   whose steps are totally included within another hit  
                   reaction which is displayed  
 RX ----- Hit Reactions (Map, Diagram, Summary for all hit reactions)  
 RXG ----- Hit Reaction Graphics (Map and Diagram for all hit reactions)  
 RXL ----- Hit Reaction Long (Map, Diagram, Summary for all hit reactions)  
 RXS ----- Hit Reaction Summaries (Map and Summary for all hit reactions)  
 SPATH ----- Reaction Map and Reaction Diagram for the "short  
                   path". Displays all single step reactions which  
                   contain a hit substance. Also displays those  
                   multistep reactions that have a hit substance in both  
                   the first and last steps of the reaction, except for  
                   those hit reactions whose steps are totally included  
                   within another hit reaction which is displayed

To display a particular field or fields, enter the display field  
 codes. For a list of the display field codes, enter HELP DFIELDS  
 at an arrow prompt (=>). Examples of combinations include: D TI;  
 D BIB RX; D TI, AU, FCRD. The information is displayed in the same order  
 as the specification. All of the formats, except CRD, CRDREF, FHIT, PATH,  
 FPATH, SPATH, FSPATH, FCRD, FCRDREF, HIT, RX, RXG, RXS, SCAN, and OCC, may  
 be used with the DISPLAY command to display the record for a specified  
 Accession Number.

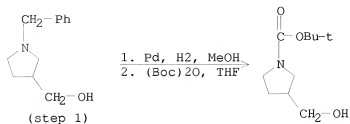
ENTER DISPLAY FORMAT (FCRDREF):  
 ENTER DISPLAY FORMAT (FCRDREF):.



10/513699

L10 ANSWER 1 OF 1 CASREACT COPYRIGHT 2008 ACS on STN

RX(7) OF 275



REF: Bioorganic & Medicinal Chemistry Letters, 12(21), 3235-3238; 2002

NOTE: isopropanol may also be used as a solvent in the first stage

10/513699

=> d his

(FILE 'HOME' ENTERED AT 11:16:01 ON 01 FEB 2008)

FILE 'REGISTRY' ENTERED AT 11:16:18 ON 01 FEB 2008

L1 STRUCTURE UPLOADED

L2 37 S L1 FULL

FILE 'CAPLUS' ENTERED AT 11:16:56 ON 01 FEB 2008

L3 17 S L2 FULL

L4 17 S L3 AND PY<2003

FILE 'CASREACT' ENTERED AT 11:30:01 ON 01 FEB 2008

L5 STRUCTURE UPLOADED

L6 10 S L5

L7 197 S L5 FULL

L8 93 S L7 AND PY<2003

L9 0 S L8 AND ORGANIC SOLVENT

L10 1 S L8 AND SOLVENT

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
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FULL ESTIMATED COST	140.47	423.89
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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CA SUBSCRIBER PRICE	-0.75	-14.35
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FILE 'STNGUIDE' ENTERED AT 11:36:23 ON 01 FEB 2008

USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

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FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Jan 25, 2008 (20080125/UP).

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
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FULL ESTIMATED COST	0.12	424.01
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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CA SUBSCRIBER PRICE	0.00	-14.35
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STN INTERNATIONAL LOGOFF AT 11:37:24 ON 01 FEB 2008